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(54) Title: RECYCLABLE METATHESIS CATALYSTS

(57) Abstract: Highly active, recoverable and recyclable transition metal-based metathesis catalysts and their organometallic complexes including dendrimeric complexes are disclosed, including a Ru complex bearing a 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene and styrenyl ether ligand. The heterocyclic ligand significantly enhances the catalytic activity, and the styrenyl ether allows for the easy recovery of the Ru complex. Derivatized catalysts capable of being immobilized on substrate surfaces are also disclosed. The present catalysts can be used to catalyze ring-closing metathesis (RCM), ring-opening (ROM) and cross metatheses (CM) reactions, and promote the efficient formation of various trisubstituted olefins at ambient temperature in high yield.

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**RECYCLABLE METATHESIS CATALYSTS****RELATED APPLICATIONS**

This application claims the benefit of U.S. Provisional Application No. 60/224,305 filed  
5 on August 10, 2000 and U.S. Provisional Application No. 60/264,361 filed on January 26, 2001.

**GOVERNMENT SUPPORT**

This invention was supported by a grant from the National Science Foundation. The government has certain rights in this invention.

**BACKGROUND OF THE INVENTION**

10 Metal-catalyzed olefin metathesis reactions serve as a springboard for the development of a range of regioselective and stereoselective processes. These processes are important steps in the chemical synthesis of complex organic compounds and polymers. In particular, these reactions often are crucial steps in medicinal chemistry for small molecule synthesis. Organo-metallic catalysts, particularly transition metal complexes based on osmium, ruthenium or  
15 tungsten, are used in many such organic transformation reactions.

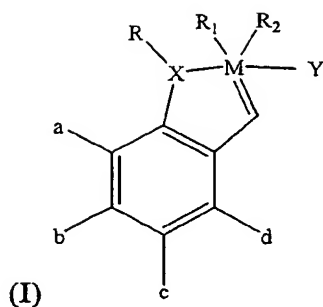
The synthesis and catalytic activity of ruthenium-based complexes which can efficiently catalyze ring-opening metathesis (ROM) and ring-closing metathesis (RCM) of dienes that contain terminal olefins has been reported for example, by Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, 121, 791-799; Harrity, J. P. A.;  
20 Visser, M. S.; Gleason, J. D.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, 119, 1488-1489; and Harrity, J. P. A.; La, D. S.; Cefalo, D. R.; Visser, M. S.; Hoveyda, A.H. *J. Am. Chem. Soc.* **1998**, 120, 2343-2351. Because of the risk of metal contamination of the resulting product, and due to the cost of organometallic catalysts, recovery and reuse of such catalysts is important. Kingsbury, et al. showed that an organometallic ruthenium-based catalyst could be recovered

from the reaction mixture by silica gel chromatography in high yield and reused in subsequent C-C bond forming reactions. Kingsbury et al., *supra*. However, there are several shortcomings in the prior art recyclable metathesis catalyst, including that it is useful mostly for substrates that contain terminal alkenes. In certain cases, due to co-elution, isolation of the catalyst from the substrate is problematic.

## SUMMARY OF THE INVENTION

The present invention comprises highly active and recyclable transition metal-based metathesis catalysts, methods of making such catalysts and their use in metathesis reactions. The catalysts of the present invention are organometallic complexes of a transition metal comprising an organic ligand that permits recovery of the catalyst metal from the reaction mixture. The organometallic complexes of the invention can be in monomeric, polymeric and dendritic forms that are capable of promoting various forms of metathesis reactions in a highly efficient manner, and can be efficiently recovered from the reaction mixtures and reused; they are therefore, recyclable. Unlike prior recoverable transition metal-based complexes, the catalysts of the present invention effect the efficient formation of trisubstituted alkenes and tetrasubstituted olefins through catalytic metathesis processes. The polymeric and dendritic catalysts of the invention offer the added advantage that they are more readily isolable. The present catalysts are extremely active (can be used to prepare tri- and tetra-substituted olefins), can be readily recovered and reused and leave little or no trace of toxic metal contamination within the product.

In one aspect, the invention comprises a composition comprising a monomeric catalyst having the following Formula I:



wherein:

M is a transition metal;

X comprises oxygen (O), sulfur (S), nitrogen (N) or phosphorus (P);

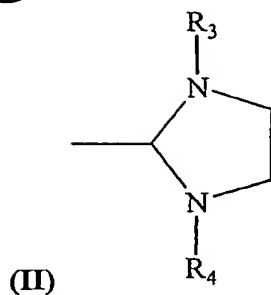
5 R comprises an alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, alkoxy carbonyl, alkylamino, alkylthio, alkylsulfonyl, alkylsulfinyl; each optionally substituted with an alkyl, halogen, alkoxy, aryl or heteroaryl moiety;

R<sub>1</sub> and R<sub>2</sub> each comprise, or together comprise, an electron withdrawing anionic ligand;

10 a, b, c, and d each comprises H, a halogen atom or an alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, alkoxycarbonyl, alkylamino, alkylthio, alkylsulfonyl, alkylsulfinyl; each optionally substituted with an alkyl, halogen, aryl or heteroaryl moiety; and

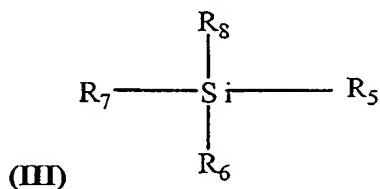
Y comprises an electron-donating heterocyclic carbene ligand.

In a preferred embodiment, M is ruthenium, X is O, R is a lower alkyl group (e.g., C<sub>1</sub>-C<sub>12</sub>), R<sub>1</sub> and R<sub>2</sub> are halogen atoms (which may be identical or different but preferably are  
15 identical), a, b, c and d each comprises hydrogen or a lower alkyl group (e.g., C<sub>1</sub>-C<sub>12</sub>), and Y comprises a 4,5-dihydroimidazol-2-ylidene carbene ligand ring structure or a phosphine moiety. In a more preferred embodiment, M is ruthenium, X is O, R is isopropyl, R<sub>1</sub> and R<sub>2</sub> are chlorine atoms (Cl), a, b, c and d each comprises hydrogen, and Y comprises a heterocyclic ring structure having the following Formula II:

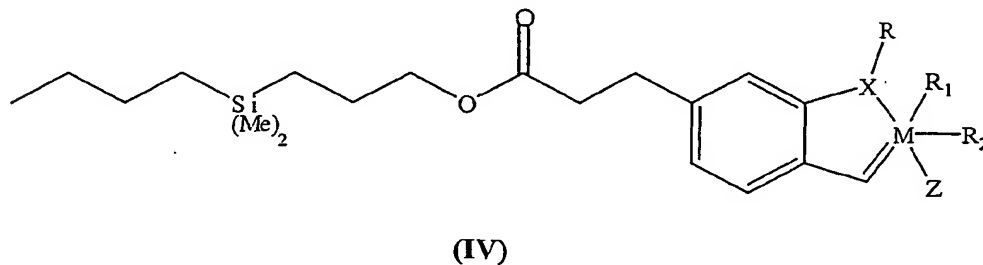


wherein  $R_3$  and  $R_4$  comprise the same or different aromatic ring moieties. In a currently preferred embodiment,  $R_3$  and  $R_4$  both comprise 2,4,6-trimethylphenyl (mesityl) moieties.

In another aspect, the invention comprises a dendritic catalyst structure having the following Formula III:



wherein  $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  each comprises the following Formula IV:



wherein:

M comprises a transition metal;

X comprises O, S, N or P;

R comprises an alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, alkoxy carbonyl, alkylamino, alkylthio, alkylsulfinyl, alkylsulfonyl; each optionally substituted with an

alkyl, halogen, aryl or heteroaryl moiety;

R<sub>1</sub> and R<sub>2</sub> each comprises, or together comprise, an electron withdrawing group; and Z comprises Y or a phosphine group.

In a preferred embodiment, M is Ru, X is O, R is a lower alkyl group (e.g., C<sub>1</sub>-C<sub>12</sub>), R<sub>1</sub> and R<sub>2</sub> are halogen atoms (which may be identical or different but preferably are identical), and Z  
5 comprises a phosphine moiety having the formula P(Cy)<sub>3</sub>, wherein Cy comprises an aliphatic ring structure, preferably cyclohexyl or cyclopentyl. In a currently preferred embodiment, M is Ru, X is O, R is isopropyl, R<sub>1</sub> and R<sub>2</sub> each is a chlorine atom (Cl), and Z is P(cyclohexyl)<sub>3</sub>.

In another preferred embodiment, M is Ru, X is O, R is a lower alkyl group (e.g., C<sub>1</sub>-C<sub>12</sub>), R<sub>1</sub> and R<sub>2</sub> are halogen atoms and Z comprises a ring structure having Formula II wherein R<sub>3</sub> and  
10 R<sub>4</sub> comprise the same or different aromatic ring moieties. In a currently preferred embodiment, M is Ru, X is O, R is isopropyl, R<sub>1</sub> and R<sub>2</sub> are chlorine atoms (Cl) and Z comprises a ring structure having Formula II wherein R<sub>3</sub> and R<sub>4</sub> both comprise a 2,4,6-trimethyl phenyl (mesityl) moiety.

The present invention provides stable, readily recoverable transition metal-based  
15 metathesis catalysts with high catalytic activity. The catalysts may be used free in the reaction mixture or may be immobilized on a solid phase. In another aspect of the invention, the monomeric catalysts of Formula I are immobilized on a solid phase. In a preferred embodiment, the catalysts of the invention are immobilized on solid phases such as, for example, metals, glass, polymers, ceramics, organic polymer beads, inorganic sol-gels or other inert substances,  
20 without impairing their ability to catalyze various forms of metathesis reactions in a highly efficient manner. In a currently preferred embodiment, the solid phase is an inorganic sol gel such as, for example, a glass monolithic gel. In addition, the invention comprises the design and synthesis of various chiral versions of the present monomeric and dendritic complexes and their application to asymmetric catalytic metathesis.

Immobilization of catalysts of the invention to an inorganic monolithic gel provides the following advantages over immobilization of such catalysts on conventional solid phases such as organic polymer beads : (1) overcomes limitations of organic polymer beads such as variable swelling and shrinking in different media, often resulting in reduction of catalytic activity

5 (2) precludes the addition of significant volumes of solvents needed for recovery of beads bound to the catalyst, a necessity that seriously limits the utility of recoverable surface immobilized catalysts, thereby detracting from the practicality of such an approach and rendering it more costly and environmentally less friendly. (3) The high porosity characteristic of inorganic gels translates to a substantially large interfacial surface area (typically 300-1000 m<sup>2</sup>/g), rendering

10 such materials ideal for immobilization of catalysts of the invention. (4) Gelation occurs after a sol is cast into a mold; it is, therefore, possible to tailor the gel samples to a desired shape or even function.

In another preferred embodiment, the surface immobilized catalysts of the present invention is an integral part of the reaction apparatus itself, thus obviating the need for a

15 filtration step to recover the catalyst after completion of metathesis processes. Processes of the present invention are, therefore, rendered operationally simple from the standpoint of both execution and work-up.

The recyclable catalysts of the present invention are substantially more active than prior art recyclable metathesis catalysts. The transition metal-based monomers and dendrimers of the

20 present invention are easily characterizable and serve as homogeneous metathesis catalysts that are highly active and allow for significantly more facile catalyst recovery compared to prior art catalysts.

## BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows two prior art ruthenium catalysts: (1) is a recoverable complex of

25 ruthenium with an isopropoxystyrene and a phosphine moiety, and (2) is a benzylidene catalyst.

Figure 2 shows an ORTEP diagram of  $\text{C}_{12}\text{Ru}(=\text{CH}-o\text{-OiPrC}_6\text{H}_4)(4,5\text{-dihydrolMES})$  (Formula 5). Thermal ellipsoids are drawn at 30% probability level, and selected bond distances and angles are shown in Table 1.

Figure 3 shows the transition metal catalysts (1, 2) and organometallic compound 2a comprising an active metal complex.

Figure 4 shows surface immobilized catalysts of the invention coupled to a solid phase (represented by a spherical solid substrated) via different types of linkers.

### DETAILED DESCRIPTION OF THE INVENTION

The present invention comprises a novel class of recoverable and recyclable organometallic metathesis catalysts. The term "recoverable" as used herein means that the catalyst can be recovered or retrieved from the reaction mixture once the reaction is complete. The term "recyclable" means that the recovered catalyst can be reused in subsequent metathesis reactions after recovery from the previous reaction(s).

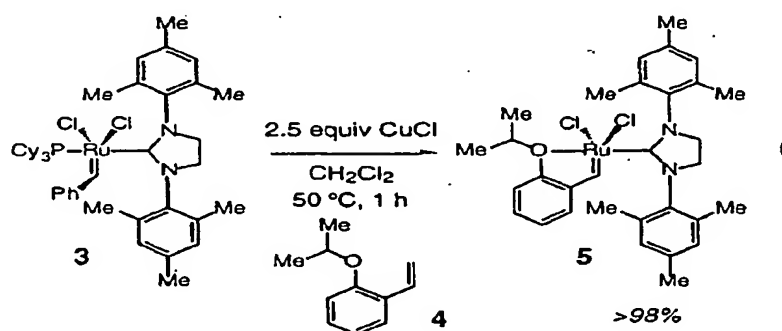
The catalysts of the present invention comprise novel monomeric catalysts having the structure of Formula I, and dendritic catalysts having the structure of Formula III. The present monomeric and dendritic catalysts are recoverable and recyclable, and can efficiently catalyze a variety of olefin metathesis reactions, including ring-opening metathesis (ROM), ring-closing metathesis (RCM), cross-metathesis (CM), ring-opening polymerization metathesis (ROMP), and acyclic diene metathesis (ADMET). The catalysts of the present invention can be used in most metathesis reactions under appropriate conditions. Those skilled in the art would be able to empirically determine the amount of catalyst and optimal conditions of the reaction. For example, the monomeric and dendritic catalysts of the present invention can be used in most reactions at levels of from about 1.0 mol% to about 5.0 mol %.



The present catalysts can be recovered from the reaction mixture by any technique suitable for recovering or separating organometallic complexes, including chromatography or filtration. For example, the monomeric or dendritic catalysts may be separated from the reaction mixture by silica gel chromatography. If the catalyst is attached to a solid phase, as described below, then the catalyst can be recovered by separating the solid phase from the reaction mixture by simple filtration.

**Monomeric complexes.** In one aspect, the present invention provides monomeric catalysts having the structure shown as Formula I. Monomeric catalysts having Formula I can be prepared according to the procedures shown in Equation 1 below, in Examples 1-10, or via other synthetic routes that would be readily ascertainable by those skilled in the art.

The structure shown as Formula 5 in Equation 1 below comprises a currently preferred embodiment of the present invention.



Equation 1

**Synthesis of Formula 5.** The catalyst of Formula 5 was synthesized and characterized, and its reactivity and recyclability were determined. It was determined that the saturated imidazolin-2-ylidene and unsaturated imidazol-2-ylidene carbene ligands accelerated the metathetic activity of Ru-based complexes. As depicted in Equation 1, treatment of compound 3 with 2.5 equivalents CuCl and 0.97 equivalents of compound 4 in CH<sub>2</sub>Cl<sub>2</sub> at 40°C delivers the

Formula 5 catalyst within 1 hour; the Formula 5 catalyst was isolated as an air stable green solid in quantitative (>98%) yield after silica gel chromatography (mp = 178-181° C dec).

Single-crystal X-ray structure analysis of a Formula 5 catalyst is shown in Figure 2; (IMES = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene). The crystal structure analysis confirms the structural assignment shown in Formula 5. Selected bond lengths and angles for Formula 5 are provided in Table 1. The overall geometry around the transition metal center and most of the bond angles and bond lengths in Formula 5 are analogous to their related values in the complex of Formula 6 (shown in Scheme 1).

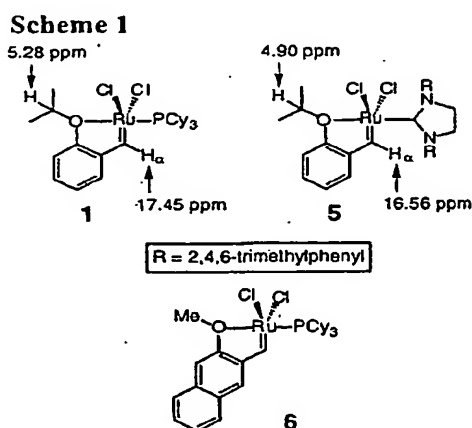
Comparison of the <sup>1</sup>H NMR spectra of prior art compound 1 (shown in Figure 1) and the Formula 5 catalyst show some of the differential structural attributes of these complexes. As illustrated in Scheme 1, there are two distinct chemical shift changes in the 400 MHz <sup>1</sup>H NMR spectra of Formula 5 catalyst and compound 1. One variation is observed at the *iso*-Pr methine proton and another at the carbene CH (H<sub>α</sub>). In both instances, the protons for the imidazolin-2-ylidene system in Formula 5 are more shielded. These differences may be attributed to higher electron density at the transition metal center of Formula 5, caused by the stronger electron donation by the heterocyclic ligand (compared to PCy<sub>3</sub> (Cy is an aliphatic cycloalkyl moiety, preferably cyclohexyl). The weaker electron donation by the oxygen ligand to the Ru center in Formula 5 may be manifested by the more upfield appearance of the isopropyl methine proton (5.28 vs 4.90 ppm).

**Table 1.** Selected Bond Lengths and Angles for  
Cl<sub>2</sub>Ru(=CH-*o*-OiPrC<sub>6</sub>H<sub>4</sub>)(4,5-dihydroIMES) (Formula 5)

Bond lengths (Å)			
Ru(1)-C(1)	1.828(5)	Ru(1)-Cl(1)	2.328(12)

Ru(1)-C(2)	1.981(5)	Ru(1)-Cl(2)	2.340(12)
Ru(1)-O(1)	2.261(3)	C(2)-N(1)	1.351(6)
		C(2)-N(2)	1.350(6)
Bond angles (deg)			
C(1)-Ru(1)-O(1)	79.3(17)	O(1)-Ru(1)-Cl(1)	86.9(9)
C(1)-Ru(1)-C(2)	101.5(14)	O(1)-Ru(1)-Cl(2)	85.3(9)
C(2)-Ru(1)-O(1)	176.2(14)	C(2)-Ru(1)-Cl(1)	96.6(12)
C(1)-Ru(1)-Cl(1)	100.2(15)	C(2)-Ru(1)-C(2)	90.9(12)
C(1)-Ru(1)-Cl(2)	100.1(15)	Cl(1)-Ru(1)-Cl(2)	156.5(5)
		N(1)-C(2)-N(2)	106.9(4)

Comparison of the  $^1\text{H}$  NMR spectra of prior art compound 1 (shown in Figure 1) and Formula 5 shows some of the structural attributes of these complexes. As illustrated in Scheme 1, there are two distinct chemical shift changes in the 400 MHz  $^1\text{H}$  NMR spectra of Formula 5 and compound 1.



One variation is observed at the *iso*-Pr methine proton and another at the carbene CH ( $H_\alpha$ ). In both instances, the protons for the imidazolin-2-ylidene system in Formula 5 are more shielded. These differences may be attributed to higher electron density at the transition metal center of Formula 5, caused by the stronger electron donation by the heterocyclic ligand (compared to PCy<sub>3</sub> (Cy is an aliphatic cycloalkyl moiety, preferably cyclohexyl). The weaker electron donation by the oxygen ligand to the Ru center in Formula 5 may be manifested by the more upfield appearance of the isopropyl methine proton (5.28 vs 4.90 ppm).

**Catalytic Activity and Recovery of Formula 5 catalyst.** The data in Table 2 below illustrate that the Formula 5 catalyst is an effective catalyst for RCM of dienes. In this reaction, hetero- and carbocyclic compounds bearing trisubstituted alkenes were obtained from the corresponding precursor dienes in the presence of 5 mol % catalyst at ambient temperature within 10 min to 2 h. As shown in entries 1 and 2 of Table 2, both 1,1-disubstituted (7) and trisubstituted olefins (9) may be utilized in the synthesis of trisubstituted cyclic alkenes. The catalytic RCM in entries 3-4 indicate that trisubstituted allylic alcohols (12) and acetates (14) can be accessed in the presence of 5 mol % 5 within 2 h. The Ru catalyst of Formula 5 is recovered with high efficiency (95% and >98% yield, respectively). The prior art catalyst 1 is significantly less efficient in promoting the above transformations. As an example, treatment of structure 11 with 5 mol % 1 (22 EC, CH<sub>2</sub>Cl<sub>2</sub>) leads to only 15% conversion after 2 h (as judged by 400 MHz <sup>1</sup> NMR).

Two important points in connection to the above data are important:

(1) In all instances, the catalyst is recovered, along with the desired cyclic product in high yield after simple silica gel chromatography. Moreover, addition of 2 equivalents of styrene ether 4 (relative to the catalyst) to a solution of a transformation promoted by the non-recyclable 3 at the end of the reaction time, leads to the isolation of the recyclable catalyst 5. As an example: Treatment of diene carbinol 11 is treated with 5 mol % 3 (CH<sub>2</sub>Cl<sub>2</sub>, 22EC, 1 h),

followed by the addition of 10 mol % 4 and addition stirring for 1 h, leads to the formation of 12 and 5 in 98% and 82% yields, respectively (after silica gel chromatography).

(2) Catalyst loading lower than 5 mol % is sufficient. As exemplified by the reaction in entry 2, catalytic RCM can readily proceed to completion with only 1 mol % Formula 5 catalyst. As another example, catalytic RCM of 7 occurs within 10 min at 22°C in the presence of 1 mol % of 5 to afford 8 in 73% isolated yield (>98% conv); recovered 5 is obtained in 92% yield after chromatography.

As the reaction in entry 5 of Table 2 indicates, tetra-substituted olefins can also be obtained through catalytic RCM promoted by the catalyst of Formula 5.

**Table 2. Ring-Closing Metathesis of Acyclic Dienes by Ru Complex 5 <sup>a</sup>**

entry	substrate	product	time	conv (%)	product yield (%) <sup>b</sup>	catalyst recovery (%) <sup>b</sup>
1			10 min	>98	82	98
2			20 min	>98	87	98
3			2 h	>98	75	95
4			1.5 h	>98	82	>98
5			44 h	42	38	81
6			30 min	70	65	60

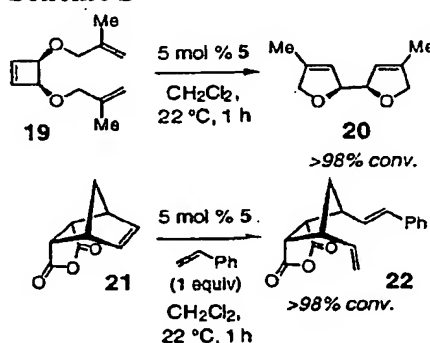
<sup>a</sup>Conditions: 5 mol % 5 for entries 1 and 3-6, 1 mol % 5 for entry 2, 22° C, CH<sub>2</sub>Cl<sub>2</sub> (entries 1-4); 24 h at 22 EC and 20 h at 40EC, CH<sub>2</sub>Cl<sub>2</sub> for entry 5; toluene, 80°C for entry 6.

<sup>b</sup>Isolated yields after silica gel chromatography.

In this instance, the Ru catalyst is recovered in >80% yield. When toluene is used as the solvent in the catalytic RCM of compound 17, tetrasubstituted alkene 18 is formed in 65% isolated yield within 30 minutes (70% conversion).

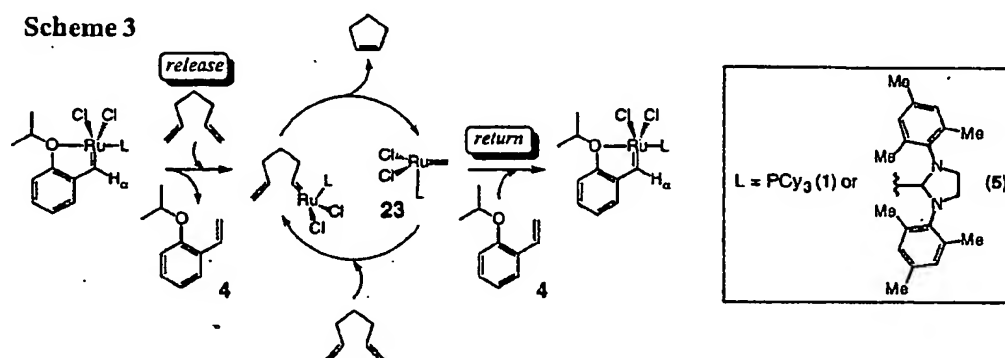
The catalysts used the above-described transformations may be retrieved from the reaction mixture, e.g., using silica gel chromatography, and then may be used in subsequent metathesis reactions with equal efficiency and without recrystallization. For example, the catalyst recovered from the reaction in entry 1 of Table 2 was reused in the same reaction to afford the desired product 8 in 71% isolated yield (10 minutes, 22 °C). The Formula 5 catalyst was again recovered in 98% yield after chromatography.

**Scheme 2**



As shown by the representative transformations in Scheme 2, Formula 5 also is an efficient catalyst in ROM / RCM and ROM / CM processes. Both transformations were completed within 1 hour, with >98% conversion.

Scheme 3 shows the release/return mechanism by which the present monomeric catalysts function as metathesis catalysts. As shown therein, a diene substrate probably first reacts with the initial Ru complex to remove the transition metal from the styrene ligand and "release" the styrene ether 4. Upon consumption of the diene, the active Ru-carbene reacts with the previously occupied styrenyl ether to cause reformation or "return" of the initial complex.

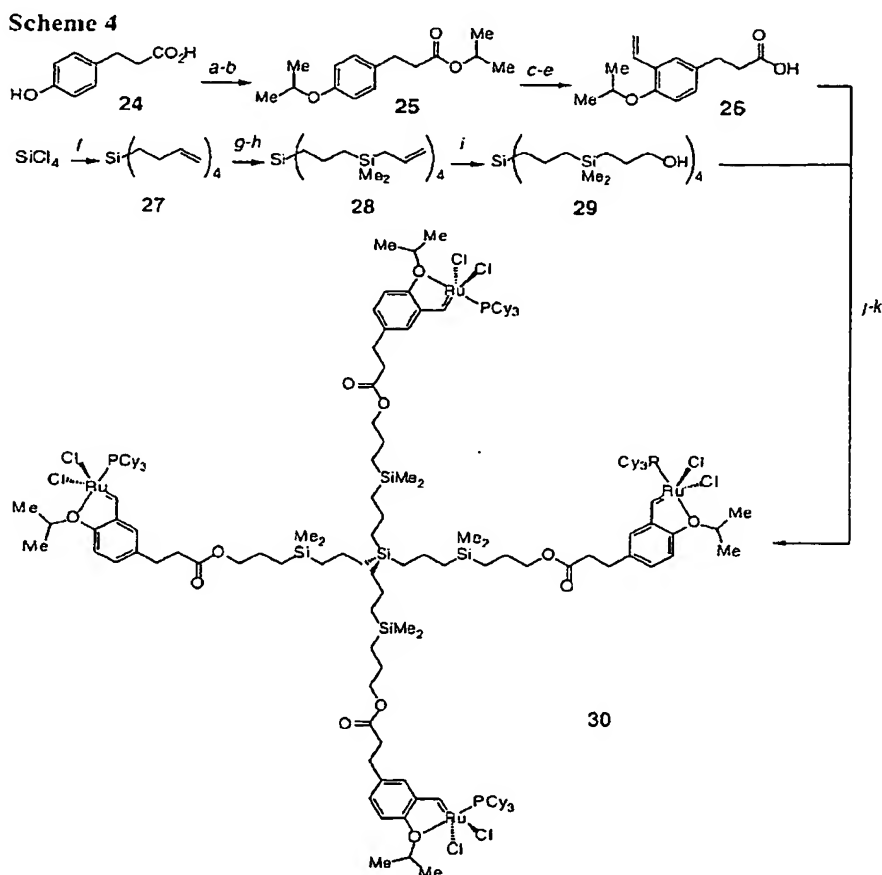


**Dendritic complexes.** In another aspect, the present invention provides dendritic catalysts having the structure shown as Formula III. Dendritic catalysts having Formula III can be prepared according the procedures described below, in Examples 11-16, or via other synthetic routes that would be readily ascertainable to these skilled in the art.

The structures shown as Formulae 30 and 31 below comprise currently preferred embodiments of the present invention.

Dendritic complexes, due to their different polarity compared to the monomeric species, generally can be more easily separated from reaction products. With dendrimers, it is possible to gauge more rigorously the efficiency with which the active metal-carbene leaves the ligation site and returns to the catalyst macromolecule. In addition both the release of the metal center from the styrenyl ligand (initiation) and the return of the active metal to the initial site (recovery), which is shown in Scheme 3 above, are more efficient with the more accessible and exposed terminal sites within the dendrimer structure.

**Synthesis of Ru-Containing Dendrimers.** In a currently preferred embodiment, the dendrimers are tetraalkylsilyl systems. Scheme 4 below shows a synthetic scheme for synthesizing a preferred Ru-containing dendrimer (Formula 30).



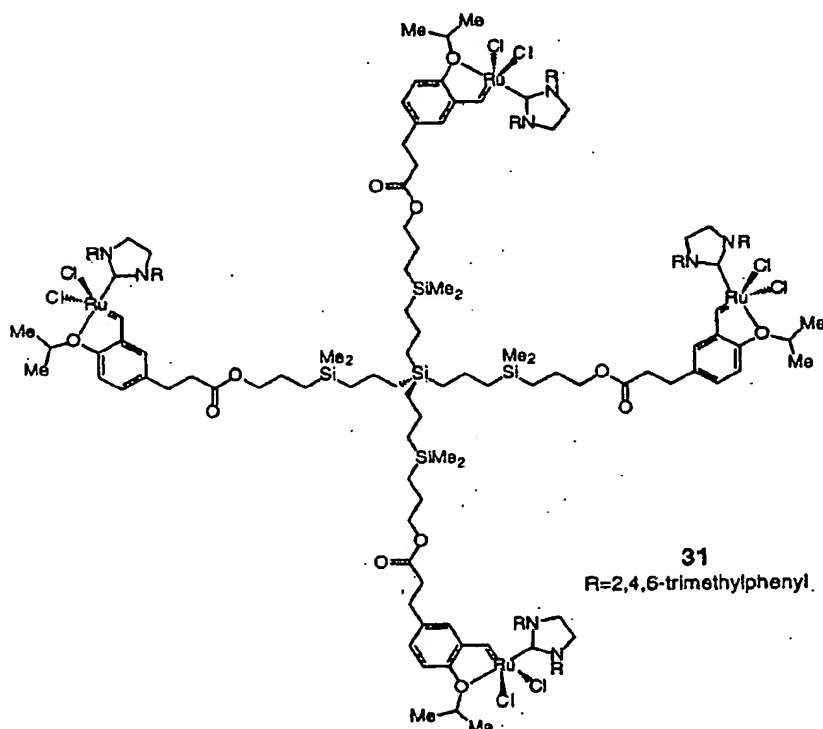
- 5 a. anhydrous HCl, i-PrOH, >87%, b, 2 equiv NaH, 2 equiv i-PrI, DMF, THF, 89%. c. 1.1 equiv Br<sub>2</sub>, HOAc, CH<sub>2</sub>Cl<sub>2</sub>, 98%. d. 1.1 equiv Bu<sub>3</sub>SnCHCH<sub>2</sub>, 3 mol % Pd(PPh<sub>3</sub>)<sub>4</sub>, 2 mol % BHT, tol, 110 °C, 4h, >98%. g. 4.3 equiv Hme<sub>2</sub>SiCl, 5 mol % H<sub>2</sub>PtCl<sub>6</sub> in THF, 3h. h. 4.2 equiv CH<sub>2</sub>CHCH<sub>2</sub>MgBr, Et<sub>2</sub>O, 22 °C, 3h, >90% overall for two steps. i. 5.1 equiv 9-BBN, THF, 22 °C, 17 h; NaOH, H<sub>2</sub>O<sub>2</sub>, EtOH, THF, 22 °C, 6 h, 96%. J. 4.9 equiv EDC·HCl, 4.5 equiv 26, 0.6
- 10 equiv DMAP, 22 °C, 3 h, 63%. k. 4.3 equiv 2, 4.6 equiv CuCl, CH<sub>2</sub>Cl<sub>2</sub>, 22 °C, 3 h, 83%.

The key features of the synthesis shown in Scheme 4 include the attachment of the requisite vinyl group through a palladium (Pd)-catalyzed Stille coupling ( 26) and preparation



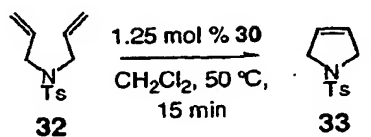
of the dendrimer backbone by a platinum (Pt)-catalyzed hydrosilation / alkylation / hydroboration sequence (27 28 29). Coupling of 29 with four equiv 26, followed by incorporation of the Ru center through treatment with 2 in the presence of CuCl affords the desired 30 as an air stable brown solid (mp = 92-98 °C dec.).

- 5 Another preferred Ru-containing dendrimer, Formula 31, can be prepared as an air stable dark green solid by the same sequence of reactions as shown in Scheme 4, except that the last step involves treatment of the vacant dendritic structure with 4.3 equiv 3 and 4.6 equiv CuCl in CH<sub>2</sub>Cl<sub>2</sub> for 10 mm (55% yield; mp = 114-117°C dec).



- 10 **Catalytic RCM, ROM and CM Promoted by Dendritic Catalysts of Formulae 30 and 31.** Table 3 below illustrates the use of the present dendritic catalysts in a RCM reaction. As shown in Table 3, treatment of diene 32 with 1.25 mol % of 30 (5 mol % Ru) leads to efficient and catalytic RCM. The desired product (33) is first isolated in 99% yield by silica gel chromatography through elution with CH<sub>2</sub>Cl<sub>2</sub> subsequent wash of the silica with Et<sub>2</sub>O leads to
- 15 the isolation of the dendritic catalyst (>98% mass balance). Recovered 30 was analyzed by 400

MHz  $^1\text{H}$  NMR spectroscopy; the resulting spectrum indicated that 13% of the styrenyl ligands were vacant (approximately 13% Ru loss).



**Table 3.** Utility of Dendritic Catalyst Formula 30 in Catalyzing RCM

Cycle	product yield <sup>a</sup>	Ru content <sup>b</sup>
	(%)	(%)
1	99	87
2	91	76
3	96	72
4	89	64
5	92	48
6	87	41

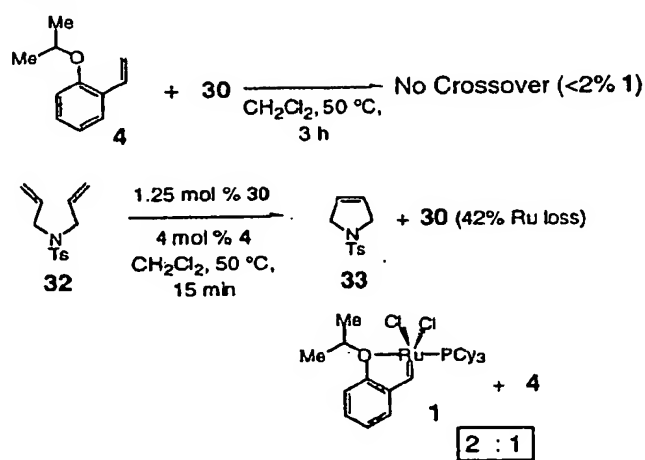
<sup>a</sup>Isolated yields after silica gel chromatography.

<sup>b</sup>Determined by analysis of the 400 MHz  $^1\text{H}$  NMR of the purified reaction mixture of dendrimer after silica gel purification (devoid of other Ru-containing impurities).

As illustrated in Table 3, repeated use of Formula 30 as a catalyst results in complete conversion of 32 to 33 and isolation of the desired product in >86% isolated yield. These data thus illustrate that dendrimer 30 is effective in promoting the catalytic RCM of terminal dienes in a highly efficient manner, and can be easily recovered by simple silica gel filtration and reused repeatedly in subsequent reactions. In addition, after repeated use, the partially depleted

dendrimer complex can be easily re-metallated upon treatment with the appropriate equivalents of **3** and CuCl in CH<sub>2</sub>Cl<sub>2</sub>. The dendritic complex remains active even after nearly 50% of the Ru content has been depleted (see cycle 6 in Table 3). This level of reactivity may be attributed, at least partially, to the fact that **30** (similar to monomeric catalysts **1** and **5**) releases a highly active mono-phosphine Ru complex into the solution. In the absence of a second equivalent of PCy<sub>3</sub> that can re-coordinate to Ru and retard its catalytic activity (which is the case when **2** or **3** are used as catalysts), and since styrene ethers probably do not kinetically re-associate with Ru as efficiently as PCy<sub>3</sub>, even a small amount of Ru release can lead to substantial amounts of metathesis activity.

Scheme 5

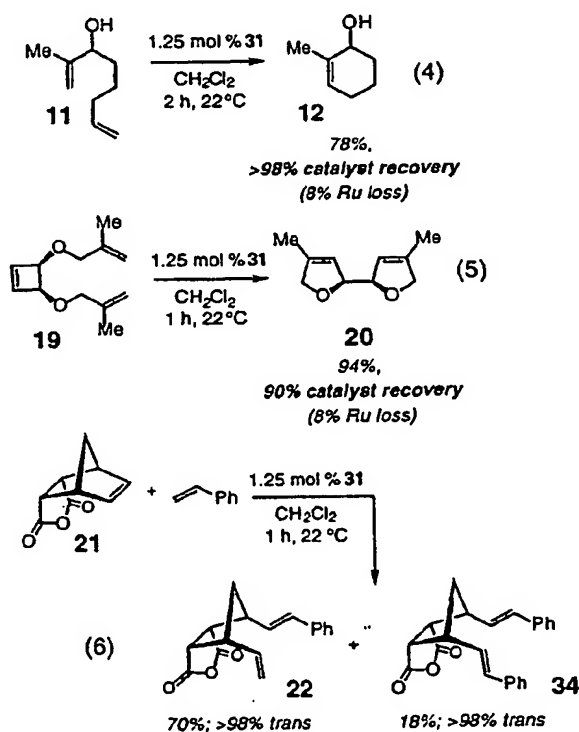


Metal crossover experiments were carried out as depicted in Scheme 5. Treatment of compound **4** with dendritic Ru complex of Formula **30** results in little or no metal crossover (<2% **1** formed by 400 MHz <sup>1</sup>H NMR analysis). The amount of Ru bound to the dendritic vs monomeric ligands is readily determined by the chemical shift difference in the <sup>1</sup>H NMR spectra of the corresponding carbene CH (Ru=C(H)). When diene substrate **32** is treated with 1.25 mol % fully loaded **30** and 4 mol % **4**, RCM product **33** is obtained within 15 min. However, recovered **30** bears 42% less Ru, compared to 13% metal reduction when the reaction is carried

out in 4 (see Table 3, cycle 1). In addition, ~30% of uncomplexed 4 is isolated after the reaction; the remainder of the monomeric styrenyl alkoxide is recovered as monomeric Ru complex 1.

These observations indicate that the Ru metal, after reacting with the diene substrate and leaving the dendrimer, can be trapped again by a styrenyl alkoxide. Thus, in the absence of compound 4,

the catalytically active Ru monophosphine would likely return to a styrene unit within the dendritic structure.



Scheme 6

Dendrimer 31 exhibits catalytic activity higher than that observed for 30. Unlike 1 or 30, but similar to 5, dendritic 31 efficiently promotes the formation of trisubstituted allylic alcohol 12 (Scheme 4); in addition to the desired product (78%), the dendrimer is recovered after silica gel chromatography quantitatively with 8% loss in Ru loading (judged by analysis of 400 MHz  $^1\text{H}$  NMR). Moreover, as shown in Equation (5), similar to 5, dendrimer 31 effectively catalyzes tandem ROM / RCM of 19 and the formation of 20 (94%). However, in contrast to the

corresponding monomer 5, dendrimer 31 can be easily separated from 20 and recovered in 90/s yield (8% Ru loss). The transformation in **Scheme 6** indicates that 31 effectively promotes catalytic ROM / CM reactions as well, and as before, it can be recovered readily and in good yield (>98% trans olefins in 22 and 34, as judged by 400 MHz <sup>1</sup>H NMR analysis). Thus,

5 dendritic catalyst 31 retains the high activity of monomeric 5 and provides the valuable practical advantage of being readily separable from metathesis products.

Similar to monomeric 5, lower loadings of 31 are sufficient for efficient catalytic metathesis. As an example, when triene 7 is treated with 0.25 mol % 31 (CH<sub>2</sub>Cl<sub>2</sub>, 22°C) for 10 min, RCM adduct 8 is formed with >98% cony. In addition to dihydrofuran 8, isolated in 84%  
10 yield, recovered 31 is obtained in 88% yield after silica gel chromatography (22% Ru loss).

**Immobilization of the Catalysts on a Solid Phase.** The present catalysts can be attached to or immobilized on a solid support for use in metathesis reactions. Solid phases which can be used include, for example, metals (including magnetic media), glass, polymers, ceramics or other inert substances that will not affect the reaction. The solid phase may be in any form useful for  
15 carrying out the particular reaction, including particles, beads, rods, plates, fibers, filters, etc. Methods for attaching organometallic catalysts to solid supports and using them in metathesis reactions are known in the art. One method for attaching the preferred monomeric catalyst of the present invention to a polymer substrate is described in Example 19.

The catalysts of the present invention can be immobilized with retention of all the ligand  
20 environment characteristics responsible for its high activity. In one embodiment, the immobilized catalyst is immobilized on the solid support in a manner such that the support is a catalyst carrier. In this embodiment, the metathesis substrate releases the active metal carbene from the polymer, the complex promotes several cycles in solution, and is again trapped by the support so that it can be easily retrieved and reused. In other words, the present immobilized

catalyst systems combine the benefits of heterogeneous catalysis (recyclability) and homogeneous catalysis (high turnover).

In a preferred embodiment of the invention, the transition metal catalysts are immobilized on solid phase surfaces such as, for example, metals, glass, polymers, ceramics, organic polymer  
5 beads, inorganic sol-gels and other inert substances, without impairing their ability to catalyze various forms of metathesis reactions in a highly efficient manner. In a currently preferred embodiment, the solid phase is an inorganic sol gel such as, for example, a glass monolithic gel.

The surface immobilization of the catalysts to solid phase substrates involves a preliminary step wherein the catalysts are chemically reacted with an organic coupling agent to  
10 provide adducts that are capable of chemically bonding to said solid phase substrates. In a preferred embodiment, the said adduct contains a silyl functionality that enables surface immobilization on solid phase substrates via chemical bonding of the silyl group to the said substrates. In a most preferred embodiment the catalysts of the invention are coupled to the organic linker and functionalized with a silane-containing moiety in a single step. Surface

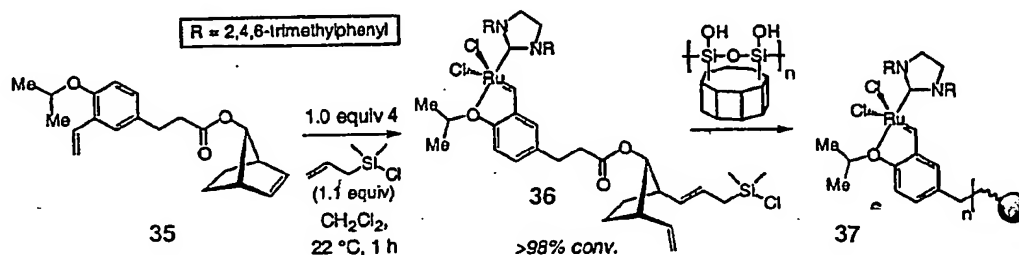
15 immobilization of the said silane modified compounds onto solid phase substrates is accomplished in-situ by subsequent addition of said substrate into the reaction vessel. Preferred coupling agents are norbornene derivatives that are capable of reacting with catalysts of the invention, and further capable of reacting with organo-silane agents to provide silyl-

functionalized derivatives that may be used in surface immobilization reactions. Preferred solid  
20 phase substrates include those capable of chemically reacting with the silyl moiety. In a most preferred embodiment, the solid phase substrate is a porous glass monolith having preferably an average pore size of about 200 Å. More specifically, as shown in Figure 4, a ring-opening reaction combined with cross metathesis of anti-norbornenol ester 35 in with 1.0 equivalent each

of organometallic complex 4 and allylchlorodimethylsilane (0.05 M CH<sub>2</sub>Cl<sub>2</sub>, 22 °C) proceeds to  
25 >98% conversion in <1 h to give adduct 36 (analyzed by 400 MHz <sup>1</sup>H NMR). Surface immobilization of adduct 36 is accomplished by adding a pre-weighed batch of vacuum-dried

sol-gel monoliths such as, for example, glass monolithic gel with about 200 Å pore size to the reaction mixture, followed by stirring for 96 h at 40 °C. After extensive washing with CH<sub>2</sub>Cl<sub>2</sub> and drying in vacuo, bright green glass pellets of surface immobilized catalyst **37** are recovered.

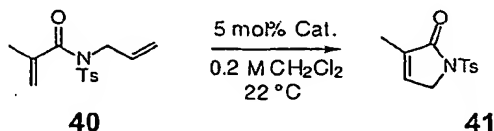
In other preferred embodiments, surface immobilized catalysts **38** and **39** shown in Scheme 7 are obtained in an analogous fashion from the corresponding norbornene substrates. Surface immobilized catalysts **35**, **36** and **37** were evaluated for catalytic activity, recovery and recyclability.



Scheme 7

All surface immobilized catalysts of the present invention show good activity in catalyzing metathesis reactions. Table 4 shows efficiency of immobilized catalysts **37**, **38** and **39** carried through iterative rounds of ring-closing metathesis (RCM) of acrylic amide **40** to yield **41**. The catalyst loading for each of these transformations was determined by the mass increases that accompany functionalization of the gel surface. Relative reaction rates of three catalysts were assessed by stopping the reaction prematurely during the third round of RCM, at a point where TLC analysis still showed the presence of a small amount of starting material. Spectroscopic analysis of the (400 MHz <sup>1</sup>H NMR) unpurified reaction mixture (97-100% conversion, Round 3, Table 4) indicates that reaction efficiency of all three catalysts tested are equivalent.

**Table 4. Utility of Immobilized Catalysts in catalyzing RCM**



Catalyst	Round 1 (3 h)	Round 2 (3 h)	Round 3 (2h)	Round 4 (3h)	Metal Loss
37	>98% conv, 99%	>98% conv, 100%	97% conv, 100%	>98% conv, 99%	1.8 mg (25%)
38	>98% conv, 100%	>98% conv, 100%	97% conv, 99%	>98% conv, 100%	1.9 mg (20%)
39	>98% conv, 99%	>98% conv, 99%	99% conv, 100%	>98% conv, 100%	1.6 mg (22%)

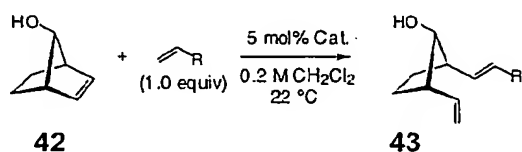
The surface immobilized catalysts of the present invention provide the following advantages over non-immobilized catalysts **1** and **2** and **2a** (Figure 3).

- (1) In contrast to reactions run with 5 mol% non-immobilized catalysts **1** and **2**, the proton NMR spectra of the unpurified reaction mixtures in every case consists of >98% pure cyclo-olefin (analyzed by 400 MHz <sup>1</sup>H NMR); no catalyst or byproduct thereof is detected). Concentration of the reaction mixtures consistently deliver the cyclo-olefins as an off-white solids in >98% yield. These materials meet the acceptance criteria as defined by CH combustion analysis without need for purification.
- (2) No post reaction filtration step is required for product isolation and catalyst recovery. The reaction mixture is removed by pipetting, decantation or pumping, following which the solid surface (for example, inorganic gel pellets such as glass) with the immobilized catalyst is washed with CH<sub>2</sub>Cl<sub>2</sub>, prior to addition of fresh substrate for a subsequent metathesis reaction.
- (3) After four consecutive rounds of RCM utilizing surface immobilized catalysts with different organic linker types, the respective gel pellets after thorough drying in vacuo and subsequent weighing yielded mass differences that are highly reproducible, indicating a net metal loss of between 20 to 25% over the four reaction cycles. Despite this significant drop in Ru catalyst loading relative to the initial values, the catalytic activities of the recovered, recycled gel pellets remain high. Absence of cross-contamination of reaction products by surface immobilized catalysts of the present invention may be demonstrated by using the same samples for the ring-opening metathesis (ROM) of 7-anti-norbornenol in the presence of a variety of



donor olefins, including highly electron-rich olefins such as vinylferrocene. As shown in Table 5, productive metathesis for three additional rounds of norborneol **42** occurred in <1 h to yield ring-opened compound **43**. The Ru-containing impurities, as well as the product of the previous RCM reaction **39** could not be detected by NMR spectroscopy (400 MHz  $^1\text{H}$  NMR analysis) of the corresponding unpurified reaction product mixtures.

**Table 5.** Efficiency of Recycled Catalysts in catalyzing ROCM



Catalyst	R=Ph Rounds 5 (40 min)	R = n-hexyl Round 5 (40 min)	R – Ferrocene Round 7 (40 min)
37	>98% conv	>98% conv	>98% conv
38	>98% conv	>98% conv	>98% conv
39	>98% conv	>98% conv	>98% conv

In addition to attaching the catalyst to a substrate such as an organic polymer bead that necessitates an additional filtration step to isolate the product from catalyst, the catalysts of the invention may be immobilized on the surface of a reaction vessel. In a preferred embodiment, the catalyst metal complex is immobilized to an integral part of the reaction apparatus itself, for example, a glass round-bottom reaction flask, a magnetic stir bar, or other component used to carry out the reaction. Catalysts of the present invention may also be attached to highly porous glass monoliths, which can be synthesized and manipulated from readily available materials.

Preferably, the linker moiety used to bind the metal complex to the solid support should be chemically inert under the reaction conditions and form a non-labile link between the metal complex and support. In one embodiment, as shown in Scheme 7, the present catalysts are

immobilized using a procedure that allows incorporation of both the linker and the active metal complex in a single step. Subsequent diffusion of the catalyst and linker into the pores of a sol gel material, for example, results in a substitution reaction involving the labile Si-C1 bond with free hydroxyl groups on the glass surface, thereby immobilizing the catalyst to the glass surface.

5 As shown in Example 19, ring-opening cross metathesis (0.10 mmol scale) of a strained olefin using the catalyst synthesized according to Example 4 (shown as Formula 3 in Equation 1 above) proceeded to >98% conversion. In this reaction, a catalyst of the present invention was immobilized on a single 50 mg sol gel monolith. After extensive washing and drying in vacuo, a bright green glass pellet was recovered which showed good activity in the RCM of the terminal  
10 diene (0.10 mmol scale). The immobilized catalyst was carried through three iterative rounds of metathesis.

The following Examples are provided to illustrate the present invention, and are not intended to be limiting in any way.

## 15 EXAMPLES

**General.** Infrared (IR) spectra were recorded on a Perkin-Elmer 781 spectrophotometer,  $\lambda_{\text{max}}$  in  $\text{cm}^{-1}$ . Bands are characterized as broad (br), strong (s), medium (m), and weak (w).  $^1\text{H}$  NMR spectra were recorded on Varian Unity 300 (300 MHz), Gemini 2000 (400 MHz), or INOVA 500 (500 MHz) spectrometers. Chemical shifts are reported in ppm from  
20 tetramethylsilane with the solvent resonance as the internal standard ( $\text{CDCl}_3$ ):  $\delta$  7.26 ppm;  $\text{CD}_3\text{CN}$ :  $\delta$  1.94 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, br = broad, m multiplet), coupling constants (Hz), integration, and assignment.  $^{13}\text{C}$  NMR spectra were recorded on Varian Unity 300 (75 MHz), Gemini 2000 (100 MHz), or INOVA 500 (125 MHz) spectrometers with complete proton decoupling. Chemical

shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference (CDCl<sub>3</sub>: 77.00 ppm; CD<sub>3</sub>CN: 1.19 ppm). <sup>31</sup>P NMR spectra were recorded on a Varian Gemini 2000 (162 MHz) spectrometer with complete proton decoupling. The chemical shifts of the phosphorus resonances were determined relative to phosphoric acid as an external standard

5 (H<sub>3</sub>PO<sub>4</sub>: δ 0.0 ppm).

All reactions were carried out under an atmosphere of dry Ar in oven- (135°C) and flame-dried glassware with standard Schlenk or vacuum-line techniques. In most instances, solid organometallic compounds were purified and recovered in air and later stored in a drybox under an atmosphere of argon. (PCy<sub>3</sub>)Cl<sub>2</sub>RuCHPh (**Formula 2**) was prepared according to literature

10 procedures.<sup>30</sup> (4,5-dihydroIMES)(PCy<sub>3</sub>)Cl<sub>2</sub>Ru=CHPh (**Formula 3**) and its requisite starting materials were prepared by a modification of the published method<sup>31</sup> (see below for further details). 2-isopropoxystyrene was prepared by alkylation and Wittig olefination. All other materials were obtained from commercial sources and purified before use. Tetrahydrofuran, diethyl ether, benzene, and toluene were distilled from sodium metal/benzophenone ketyl.

15 Dichloromethane, pentane, hexanes, 2-propanol, triethylamine, and ethanol were distilled from calcium hydride under Ar. Methanol was distilled over Mg under Ar. 2,4,6-trimethylaniline was vacuum distilled. Triethyl orthoformate (Aldrich) was distilled from MgSO<sub>4</sub> under reduced pressure. 3-(4-Hydroxyphenyl)-propionic acid (Aldrich) was recrystallized from water. 2-Iodopropane (Aldrich) was distilled from MgSO<sub>4</sub> under argon. Dimethylformamide (Fisher) was

20 stored over 4A molecular sieves prior to use. Tributyl(vinyl)tin (Aldrich) was vacuum distilled from MgSO<sub>4</sub>. Allylmagnesium bromide was freshly prepared from distilled allyl bromide (Aldrich) and Mg turnings (Strem) and titrated before use. Silicon tetrachloride (Strem) was distilled under argon. Chlorodimethylsilane (Aldrich) was distilled under argon. 9-Borabicyclo[3.3.1]nonane (9-BBN) was freshly prepared from distilled 1,5-cyclooctadiene

25 (Aldrich), borane-dimethylsulfide complex (Aldrich), and anhydrous dimethoxyethane (Aldrich, distilled from sodium metal/benzophenone ketyl).<sup>32</sup> 4-Dimethylaminopyridine (DMAP)

(Aldrich) was recrystallized from anhydrous toluene. The following materials were purchased from commercial sources and used as received: glyoxal (40% wt. soln in water) (Aldrich), sodium cyanoborohydride (Aldrich), bromocresol green (Fisher), ammonium tetrafluoroborate (Aldrich), potassium *tert*-butoxide (Strem), copper(I) chloride (Strem), anhydrous HCl (Aldrich),  
5 sodium hydride (Aldrich), bromine (Aldrich), acetic acid (Fisher), sodium thiosulfate (Aldrich), 2,6-di-*tert*-butyl-4-methylphenol (Aldrich), tetrakis(triphenylphosphine)palladium (0) (Strem), activated carbon (Aldrich), chloroplatinic acid hexahydrate (Speier's catalyst) (Strem), platinum-divinyltetramethylsiloxane complex in xylene (Karstedt's catalyst) (Geleste), hydrogen peroxide (30% wt. soln in water) (Aldrich), citric acid (Aldrich), and 1-(3-dimethylaminopropyl)-3-ethyl  
10 carbodiimide (EDC) (Advanced Chemtech).

All silica gel column chromatography was driven with compressed air and performed with silica gel 60 (230-400 mesh; pH (10% suspension) 6.5-7; surface area 500 m<sup>2</sup>/g; pore volume 0.75 ml/g) obtained from TSI Chemical Co. (Cambridge, MA). Similar to the original monomer 1, dendritic catalyst 30 forms a dark brown solution in organic solvents. In contrast,  
15 the more active catalysts bearing the 4,5-dihydroIMES ligand form bright green-colored organic solutions. The purification of the above complexes can be easily monitored visually since they appear as dark brown or green-colored bands on the column. Dendritic complexes 30 and 31 are significantly more polar than the corresponding monomers. Following a metathesis reaction mediated by 30 or 31, isolation of both product and catalyst typically involved simply a filtration  
20 of the crude mixture through a silica gel plug in 100% CH<sub>2</sub>Cl<sub>2</sub> followed by a column "flush" in 100% Et<sub>2</sub>O (TLC R<sub>f</sub> of 30 and 31 < 1.0 in CH<sub>2</sub>Cl<sub>2</sub>).

**Example 1: Synthesis of ((2,4,6-Trimethylphenyl)NCH)<sub>2</sub>.** Glyoxal (3.73 mL of a 40% weight solution in water, 32.5 mmol) was dissolved in 325 mL of reagent-grade methanol in a 500 mL flask. 2,4,6-Trimethylaniline (8.25 mL, 58.8 mmol, 1.81 equiv) was added dropwise to  
25 this solution by syringe. The mixture was stirred for 12 h at 22 °C as a bright yellow precipitate slowly formed. The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub>, dissolving the solid. The resulting

yellow solution was dried over  $\text{MgSO}_4$ , filtered, and concentrated to a yellow-orange solid residue. The unpurified product was recrystallized from anhydrous methanol (for every 10 g, 850-900 mL of MeOH was required for complete dissolution at reflux). After slow cooling to 22 °C followed by subsequent storage of the sample at -20 °C for 12 h, long canary yellow crystals formed. The product was recovered by vacuum filtration, washed with pentane, and dried under high vacuum (7.40 g, 25.3 mmol, 86%). IR (NaCl): 3005 (m), 2946 (s), 2916 (s), 2854 (m), 2725 (w), 1617 (s), 1595 (w), 1476 (m), 1438 (w), 1374 (m), 1265 (m), 1202 (s), 1141 (m), 1031 (w), 850 (s), 780 (m), 739 (s), 705 (w), 609 (w).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 8.12 (s, 2H, NCH), 6.93 (s, 4H, aromatic CH), 2.31 (s, 6H, mesityl *p*- $\text{CH}_3$ ), 2.18 (s, 12H, mesityl *o*- $\text{CH}_3$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$ 163.31, 147.29, 134.13, 128.86, 126.44, 20.83, 18.28. HRMS Calcd for  $\text{C}_{20}\text{H}_{23}\text{N}_2$ : 292.1861 ( $\text{M}-\text{H}$ ) $^+$ . Found: 291.1862. Anal. Calcd for  $\text{C}_{20}\text{H}_{24}\text{N}_2$ : C, 82.15; H, 8.27. Found: C, 81.99; H, 8.12.

**Example 2: Synthesis of ((2,4,6-Trimethylphenyl)NHCH<sub>2</sub>)<sub>2</sub>.** The bis(imine) ((2,4,6-trimethylphenyl)NCH) (7.30 g, 25.0 mmol) was suspended in 250 mL of MeOH in a 500 mL round-bottom flask. Several crystals of bromocresol green were added as a pH indicator and the mixture was cooled to 0 °C.  $\text{NaCNBH}_3$  (10.0 g, 159 mmol, 6.4 equiv) was added to the reaction mixture in one portion as a solid. Vigorous bubbling was observed and the reaction mixture turned a deep blue-green color (alkaline pH). After 10 mm concentrated HCl was added dropwise to the mixture, restoring its original yellow color. Additional reduction slowly occurred, causing the mixture to again become basic. The acidification process was repeated (typically two more times) until the yellow color persisted. The reaction mixture was warmed to 22 °C and stirred for 1 h. A solution of 2 M KOH was added dropwise until the mixture was weakly alkaline (pH = 8-9). The mixture was then diluted with water (300 mL), transferred to a separatory funnel, and washed three times with  $\text{Et}_2\text{O}$  (500 mL). The combined organic layers were washed with 800 mL of saturated solution of sodium chloride, dried over  $\text{MgSO}_4$ , filtered, and concentrated into a yellow oil. Silica gel chromatography (TLC  $R_f$  = 0.32 in 4:1 pentane:

Et<sub>2</sub>O) afforded the product as a colorless oil (7.13 g, 24.1 mmol, 96%). IR (NaCl): 3367 (br), 2996 (s), 2916 (s), 2854 (s), 2729 (w), 1612 (w), 1485 (s), 1446 (s), 1373 (m), 1344 (w), 1228 (s), 1207 (m), 1154 (m), 1110 (m), 1062 (w), 1030 (m), 1012 (m), 853 (s), 822 (w), 801 (w), 738 (m), 563 (m). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 6.85 (s, 4H, aromatic CH), 3.30 (br, 2H, NH), 3.17 (s, 4H, NCH<sub>2</sub>CH<sub>2</sub>N), 2.30 (s, 12H, mesityl *o*-CH<sub>3</sub>), 2.25 (s, 6H, mesityl *p*-CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 143.24, 131.35, 129.65, 129.38, 49.19, 20.60, 18.50. HRMS Calcd for C<sub>20</sub>H<sub>28</sub>N<sub>2</sub>: 296.2252 Found: 296.2258. Anal. Calcd for C<sub>20</sub>H<sub>28</sub>N<sub>2</sub>: C, 81.03; H, 9.52. Found: C, 81.28; H, 9.41.

**Example 3: Synthesis of 1,3-Dimesitylimidazolinium tetrafluoroborate.** A 25 mL

round-bottom flask was charged with ((2,4,6-trimethylphenyl)NHCH<sub>2</sub>)<sub>2</sub> (7.81 g, 26.4 mmol) and ammonium tetrafluoroborate (2.77 g, 26.4 mmol, 1.0 equiv). Triethylorthoformate (4.39 mL, 26.4 mmol, 1.0 equiv) was added by syringe. The flask was equipped with a reflux condenser and submerged into a preheated oil bath at 120 °C. The mixture was refluxed for 3 h and cooled to 22 °C. A tan-colored solid precipitated, leaving a cloudy suspension. This mixture was recrystallized from hot anhydrous ethanol. The resulting bright white crystals of product were recovered by vacuum filtration, washed with pentane, and dried under high vacuum (5.62 g, 14.3 mmol, 54%). Additional product could be obtained by further recrystallization of the mother liquor. IR (NaCl): 3091 (w), 2979 (br), 2941 (br), 1633 (s), 1487 (w), 1459 (w), 1393 (w), 1313 (w), 1269 (m), 1214 (w), 1092 (m), 1054 (s), 1036 (s), 965 (w), 880 (w), 852 (m). <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>CN): δ 8.14 (s, 1H, NCHN), 7.08 (s, 4H, aromatic CH), 4.43 (s, 4H, NCH<sub>2</sub>CH<sub>2</sub>N), 2.37 (s, 12H, mesityl *o*-CH<sub>3</sub>), 2.32 (s, 6H, mesityl *p*-CH<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>CN): δ 160.41 (d, <sup>1</sup>J<sub>NC</sub> = 10.3 Hz), 141.54, 136.50, 131.36, 130.61, 52.21, 21.16, 17.92. HRMS Calcd for C<sub>21</sub>H<sub>27</sub>N<sub>2</sub>: 307.2174 (cation only). Found: 307.2175. Anal. Calcd for C<sub>21</sub>H<sub>27</sub>BF<sub>4</sub>N<sub>2</sub>: C, 63.97; H, 6.90. Found: C, 63.79; H, 6.85.

**Example 4: Synthesis of (4,5-dihydrolMES)(PCy<sub>3</sub>)Cl<sub>2</sub>Ru=CHPh (formula 3).** The

ligand salt 1,3-dimesitylimidazolium tetrafluoroborate (2.94 g, 7.46 mmol, 1.2 equiv) was suspended in 50 mL of THF in a 250 mL round-bottom flask. This mixture was then treated with a solution of potassium *tert*-butoxide (840 mg, 7.49 mmol, 1.2 equiv) in 50 mL of THF via cannula at 22 °C. This mixture was immediately cannula transferred (20 mL THF used as rinse) to a second vessel containing a solution of (PCy<sub>3</sub>)Cl<sub>2</sub>Ru=CHPh (2) (5.01 g, 6.09 mmol, 1.0 equiv) in 100 mL of benzene (additional stirring of the ligand salt mixture at 22 °C prior to exposure to the Ru-carbene often resulted in incomplete conversion to the desired product). The resulting mixture was refluxed at 80 °C for 30 min and then cooled to 22 °C. All manipulations from this point forward were carried out in air with reagent-grade solvents. The solvents were removed at reduced pressure, leaving a red-brown solid residue. The crude residue was dissolved in a minimal volume of 9:1 hexanes: Et<sub>2</sub>O and loaded onto a wide plug of silica gel. Elution with the same solvent system slowly removed a pink-red band of the desired product from the column. Concentration of the product fractions in vacuo removed the more polar and volatile Et<sub>2</sub>O and resulted in spontaneous precipitation of the catalyst from hexanes as a cranberry red, microcrystalline solid (3.78 g, 4.45 mmol, 73%). These crystals were dried under high vacuum. IR (NaCl): 3057 (m), 3039 (m), 3015 (m), 2927 (s), 2850 (s), 1608 (w), 1479 (s), 1446 (s), 1421 (s), 1380 (m), 1328 (w), 1266 (s), 1243 (m), 1205 (w), 1174 (m), 1129 (w), 1036 (w), 1005 (m), 909 (m), 849 (m), 737 (s), 703 (m), 687 (m), 624 (w), 578 (w). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 19.13 (s, 1H, Ru=CHAr), 7.35 (dd, *J* = 7.8, 7.0 Hz, 2H, aromatic CH), 7.09 (m, 3H, aromatic CH), 7.01 (s, 4H, mesityl aromatic CH), 3.98 (s, 4H, N(CH<sub>2</sub>)<sub>2</sub>N), 2.80-0.70 (m, 33H, P(C<sub>6</sub>H<sub>11</sub>)<sub>3</sub>), 2.31 (s, 12H, mesityl *o*-CH<sub>3</sub>), 1.90 (s, 6H, mesitylp-CH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 293.40, 220.29 (d, <sup>1</sup>*J*<sub>CN</sub> = 76.2 Hz), 151.16, 151.11, 138.27, 137.49, 137.08, 135.06, 129.77, 127.78, 51.64 (d, <sup>1</sup>*J*<sub>CN</sub> = 71.9 Hz), 31.30 (d, <sup>1</sup>*J*<sub>PC</sub> = 15.6 Hz), 27.68 (d, <sup>1</sup>*J* = 9.8 Hz), 26.07, 21.09, 20.86, 19.88. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): δ 161.90 (s, PCy<sub>3</sub>). Anal. Calcd for C<sub>46</sub>H<sub>65</sub>Cl<sub>2</sub>N<sub>2</sub>PRu: C, 65.08; H, 7.72. Found: C, 65.18; H, 7.71.

**Example 5: Synthesis of (4, 5-dihydroIMES)Cl<sub>2</sub>Ru = CH - *o* - O - *i* - Pr C<sub>6</sub>H<sub>4</sub>**

(**formula 5**). (4,5-dihydroIMES)(PCy<sub>3</sub>)Cl<sub>2</sub>Ru=CHPh (**formula 3**) (895 mg, 1.05 mmol, 1.03 equiv) and C<sub>6</sub>Cl<sub>4</sub> (261 mg, 2.64 mmol, 2.59 equiv) were weighed into a 100 mL round-bottom flask in a glove box and dissolved in 20 mL of CH<sub>2</sub>Cl<sub>2</sub>. 2-isopropoxystyrene (**4**) (166 mg, 1.02 mmol, 1.0 equiv) was cannulated into the resulting deep red solution in 20 mL of CH<sub>2</sub>Cl<sub>2</sub> at 22 °C. The flask was equipped with a condenser and stirred at reflux for 1 h. From this point forth, all manipulations were carried out in air with reagent-grade solvents. The reaction mixture was concentrated in vacuo to a dark brown solid residue. The crude material was dissolved in a minimal volume of 2:1 pentane: CH<sub>2</sub>Cl<sub>2</sub> and loaded onto a plug of silica gel. Elution with 2:1 pentane: CH<sub>2</sub>Cl<sub>2</sub> and then 1:1 pentane: CH<sub>2</sub>Cl<sub>2</sub> removed a bright green band from the column. The column was then washed successively with straight CH<sub>2</sub>Cl<sub>2</sub> and Et<sub>2</sub>O (light green/yellow bands elute). These three fractions were pooled and concentrated to a dark green solid. This material was passed through a second silica gel plug in 1:1 hexanes:CH<sub>2</sub>Cl<sub>2</sub> (bright green band elutes). Subjection to reduced pressure removed the more volatile CH<sub>2</sub>Cl<sub>2</sub> from the product solution and resulted in spontaneous precipitation of the catalyst from hexanes as a bright green crystalline solid; drying under high vacuum afforded 635 mg (1.01 mmol, 99%) of the desired product. IR (NaCl): 2922 (br), 2853 (m), 1730 (w), 1606 (w), 1589 (m), 1575 (w), 1478 (s), 1452 (s), 1420 (s), 1397 (m), 1384 (m), 1295 (m), 1263 (s), 1217 (m), 1160 (w), 1113 (s), 1098 (w), 1035 (w), 938 (m), 852 (w), 801 (w), 746 (m), 737 (m), 580 (m). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 16.56 (s, 1H, Ru=CHAr), 7.48 (m, 1H, aromatic CH), 7.07 (s, 4H, mesityl aromatic CH), 6.93 (dd, *J* = 7.4, 1.6 Hz, 1H, aromatic CH), 6.85 (dd, *J* = 7.4, 7.0 Hz, 1H, aromatic CH), 6.79 (d, *J* = 8.6 Hz, 1H, aromatic CH), 4.90 (septet, *J* = 6.3 Hz, 1H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 4.18 (s, 4H, N(CH<sub>2</sub>)<sub>2</sub>N), 2.48 (s, 12H, mesityl *o*-CH<sub>3</sub>), 2.40 (s, 6H, mesityl *p*-CH<sub>3</sub>), 1.27 (d, *J* = 5.9 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>CHOAr). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 6296.83 (q, *J* = 61.5 Hz), 211.13, 152.04, 145.13 (d, *J*<sub>oc</sub> = 3.9 Hz), 145.09, 138.61, 129.39 (d, *J*<sub>NC</sub> = 3.9 Hz), 129.35, 129.17, 122.56, 122.11, 112.75, 74.86 (d, *J*<sub>oc</sub> = 10.7 Hz), 51.42, 30.86, 25.93, 21.08. HRMS Calcd for



$C_{31}H_{38}Cl_2N_2O^{99}Ru$ : 623.1421 Found: 623.1411. Anal. Calcd for  $C_{31}H_{38}Cl_2N_2ORu$ : C, 59.42; H, 6.11; Cl, 11.32; N, 4.47. Found: C, 59.28; H, 6.35; Cl, 11.36; N, 4.12.

**Example 6: Synthesis of Isopropyl-1-(*p*-hydroxyphenyl)propionate.** Through a stirring solution of 3-(4-hydroxyphenyl) propionic acid (24) (5.00 g, 30.1 mmol) in 2-propanol (167 mL, 72.0 equiv) was bubbled anhydrous HCl for 50 mm. The flask was sealed under Ar and stirred for 12 h at 22 °C. The solvent was removed under reduced pressure with gentle heating, leaving a thick, colorless oil. Removal of residual 2-propanol under high vacuum at 22 °C resulted in spontaneous precipitation of the desired product as a bright white crystalline solid (6.12 g, 29.4 mmol, 98%). IR (NaCl): 3412 (br), 3024 (w), 2981 (m), 2930 (w), 2873 (w), 1712 (m), 1613 (s), 1595 (m), 1519 (s), 1449 (m), 1377 (s), 1298 (m), 1266 (s), 1225 (s), 1149 (m), 1108 (s), 904 (m), 837 (m), 820 (m), 609 (m).  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.04 (d,  $J$  8.4 Hz, 2H, aromatic CH), 6.74 (d,  $J$  = 8.4 Hz, 2H, aromatic CH), 5.80 (s, 1H, ArOH), 5.00 (septet,  $J$  = 6.3 Hz, 1H,  $(CH_3)_2CHO$ ), 2.87 (t,  $J$  = 7.6 Hz, 2H,  $CH_2CO_2iPr$ ), 2.57 (t,  $J$  = 7.6 Hz, 2H,  $ArCH_2$ ), 1.20 (d,  $J$  = 6.3 Hz, 6H,  $(CH_3)_2CHO$ ).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  172.97, 154.04, 132.19, 129.28, 115.19, 68.07 (d,  $J_{oc}$  = 9.8 Hz), 36.64, 30.23, 21.85. HRMS Calcd for  $C_{12}H_{16}O_3$ : 208.1099. Found: 208.1099. Anal. Calcd for  $C_{12}H_{16}O_3$ : C, 69.21; H, 7.74. Found: C, 69.43; H, 7.88.

**Example 7: Synthesis of Isopropyl-1-(*p*-isopropoxyphenyl)propionate (25).** A solution of isopropyl-1-(*p* hydroxyphenyl)propionate (0.822 g, 3.95 mmol) in THF (10 mL) was treated via cannula with a suspension of sodium hydride (104 mg, 5.92 mmol, 1.1 equiv) in THF (10 mL) at 0 °C. After gas evolution had subsided, DMF (20 mL) and 2-iodopropane (0.40 mL, 4.0 mmol, 1.0 equiv) were syringed into the reaction mixture. The resulting suspension was stirred at 22 °C for 6 hours, at which time additional sodium hydride (71.0 mg, 2.96 mmol, 0.75 equiv) in THF (5 mL) and 2-iodopropane (0.30 mL, 3.0 mmol, 0.75 equiv) were added. This procedure was repeated if necessary until no starting material could be detected by TLC analysis

(we suspect that competing elimination of the electrophile is responsible for incomplete product conversions, requiring us to resubject the reaction mixture). The mixture was then diluted with Et<sub>2</sub>O (150 mL) and water (200 mL) and transferred to a separatory funnel. The organic layer was removed, and the aqueous layer was washed twice with Et<sub>2</sub>O (100 mL). The combined  
5 organic layers were washed with three volumes of water to remove residual DMF. The organic solution was then dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo to a pale yellow oil. The product was passed through a short column of silica gel in 7:1 hexanes:Et<sub>2</sub>O affording 811 mg (3.24 mmol, 82%) of a colorless oil (TLC R<sub>f</sub> = 0.30 in 7:1 hexanes:Et<sub>2</sub>O). IR (NaCl): 2978 (m), 2934 (w), 1731 (s), 1612 (w), 1510 (s), 1452 (w), 1383 (m), 1295 (w), 1242 (s), 1182 (m),  
10 1109 (s), 957 (w), 829 (w). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.09 (d, *J* = 8.6 Hz, 2H, aromatic CH), 6.80 (d, *J* = 8.6 Hz, 2H, aromatic CH), 5.00 (septet, *J* = 6.3 Hz, 1H, (CH<sub>3</sub>)<sub>2</sub>CHO<sub>2</sub>C), 4.50 (septet, *J* = 6.3 Hz, 1H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 2.87 (t, *J* = 7.8 Hz, 2H, CH<sub>2</sub>CO<sub>2</sub>*i*Pr), 2.55 (t, *J* = 7.8 Hz, 2H, ArCH<sub>2</sub>), 1.32 (d, *J* = 6.3 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 1.20 (d, *J* = 6.3 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>CHO<sub>2</sub>C). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 172.39, 156.12, 132.43, 129.15, 115.81, 69.86 (d, *J*<sub>OC</sub> = 3.4 Hz),  
15 67.59 (d, *J*<sub>OC</sub> = 9.8 Hz), 36.59, 30.26, 22.14, 21.88. HRMS Calcd for C<sub>15</sub>H<sub>22</sub>O<sub>3</sub>: 250.1569. Found: 250.1566. Anal. Calcd for C<sub>15</sub>H<sub>22</sub>O<sub>3</sub>: C, 71.97; H, 8.86. Found: C, 72.26; H, 9.04.

**Example 8: Synthesis of Isopropyl-1-(*m*-bromo-*p*-isopropoxyphenyl)propionate.** A 50 mL round-bottom flask was charged with isopropyl-1-(*p*-isopropoxyphenyl)propionate (25) (1.09 g, 4.34 mmol) and CH<sub>2</sub>Cl<sub>2</sub> (20 mL, 0.20 M). 10 mL of acetic acid (0.18 mmol) was added  
20 to the solution. Bromine (0.235 mL, 4.56 mmol, 1.05 equiv) was then slowly added dropwise via syringe, forming a red-colored solution. Over the course of 0.5 h, the solution gradually turned a pale yellow color as the bromine was consumed. After 1 h the reaction was quenched with 5 mL of saturated sodium thiosulfate. The mixture was diluted with water (200 mL) and Et<sub>2</sub>O (200 mL) and partitioned in a separatory funnel. The aqueous layer was washed with 2 x  
25 150 mL of Et<sub>2</sub>O. The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated to a yellow oil. This material could be purified by vacuum distillation or silica gel

chromatography (TLC  $R_f$  = 0.23 in 10:1 hexanes:Et<sub>2</sub>O) to deliver the product as a colorless oil (1.40 g, 4.25 mmol, 98%). Crucial to the success of this reaction is this use of *exactly* 1.0-1.1 equiv of bromine; an excess of the reagent leads to dibrominated adducts. If these impurities are generated, a CH<sub>2</sub>Cl<sub>2</sub>/pentane solvent system must be used as eluant to effect purification of the  
5 desired product on silica gel (TLC  $R_f$  = 0.30 in 3:2 CH<sub>2</sub>Cl<sub>2</sub>:pentane). The halogenated solvent mix also promotes a facile separation of the product and the starting material (25) in the event that the reaction does not proceed to completion (<1.0 equiv Br<sub>2</sub>). IR (NaCl) 2979 (m), 2936 (w), 1729 (s), 1604 (w), 1493 (s), 1384 (m), 1373 (m), 1281 (m), 1253 (s), 1240 (m), 1180 (m), 1140 (m), 1109 (s), 1046 (w), 954 (m), 812 (w). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.38 (d,  $J$  = 2.2  
10 Hz, 1H, aromatic CH), 7.06 (dd,  $J$  = 8.4, 2.2 Hz, 1H, aromatic CH), 6.83 (d,  $J$  = 8.4 Hz, 1H, aromatic CH), 4.96 (septet,  $J$  = 6.2 Hz, 1H, (CH<sub>3</sub>)<sub>2</sub>CHO<sub>2</sub>C), 4.50 (septet,  $J$  = 6.2 Hz, 1H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 2.85 (dd,  $J$  = 7.7, 7.3 Hz, 2H, CH<sub>2</sub>CO<sub>2</sub>iPr), 2.55 (dd,  $J$  = 7.7, 7.3 Hz, 2H, ArCH<sub>2</sub>), 1.36 (d,  $J$  = 5.9 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 1.20 (d,  $J$  = 6.6 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>CHO<sub>2</sub>C). <sup>13</sup>C  
NMR (100 MHz, CDCl<sub>3</sub>): δ 172.06, 152.84, 134.36, 133.09 (d,  $J_{OC}$  = 7.3 Hz), 128.03, 115.98,  
15 113.63, 72.34 (d,  $J_{OC}$  = 3.9 Hz), 67.80 (d,  $J_{oc}$  = 12.2 Hz), 36.29, 29.90, 22.15 (d,  $J_{oc}$  = 2.4 Hz), 21.89 (d,  $J_{oc}$  = 3.4 Hz). HRMS Calcd for C<sub>15</sub>H<sub>21</sub>BrO<sub>3</sub>: 328.0674. Found: 328.0671. Anal. Calcd for C<sub>15</sub>H<sub>21</sub>BrO<sub>3</sub>: C, 54.72; H, 6.43. Found: C, 54.84; H, 6.43.

**Example 9: Synthesis of Isopropyl-1 -(*p*-isopropoxy-*m*-vinylphenyl)propionate.**

Pd(PPh<sub>3</sub>)<sub>4</sub> (166 mg, 0.144 mmol, 3 mol %) and 2,6-di-*tert*-butyl-4-methylphenol (1 mg, 0.005  
20 mmol) were weighed into a 50 mL pear-shaped flask in a glove box and dissolved in 25 mL of dry toluene. This solution was transferred through a cannula into a neat sample of isopropyl-1-(*m*-bromo-*p*-isopropoxyphenyl)propionate (1.58 g, 4.79 mmol) in a 50 mL round-bottom flask. The resulting pale yellow solution was stirred for 15 min at 22 °C. Tributyl(vinyl)tin (1.54 mL, 5.27 mmol, 1.1 equiv) was then added dropwise to the reaction mixture through a syringe. The  
25 flask was equipped with a condenser and heated at 110 °C for 12 h. As the reaction progressed, a shiny mirror-like film of Bu<sub>3</sub>SnBr salts was gradually deposited on the walls of the flask. After

cooling to 22 °C, the reaction mixture was passed through a small plug of celite and activated carbon using Et<sub>2</sub>O as the eluant and concentrated in vacuo to give a yellow oil. Purification by silica gel chromatography (TLC R<sub>f</sub> = 0.27 in 8:1 hexanes:Et<sub>2</sub>O) afforded 888 mg of a colorless oil (3.22 mmol, 67%). IR (NaCl): 2978 (s), 2936 (m), 2873 (w), 1731 (s), 1627 (w), 1491 (s), 1373 (m), 1246 (s), 1180 (m), 1109 (s), 996 (w), 957 (m), 904 (w), 814 (w). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.31 (d, *J* = 2.3 Hz, 1H, aromatic CH), 7.07-6.99 (m, 2H, aromatic CH and ArCHCH<sub>2</sub>), 6.80 (d, *J* 8.2 Hz, 1H, aromatic CH), 5.71 (dd, *J* = 17.8, 1.6 Hz, 1H, ArCHCH<sub>2</sub>), 5.22 (dd, *J* = 11.3, 1.6 Hz, 1H, ArCHCH<sub>2</sub>), 5.00 (septet, *J* = 6.3 Hz, 1H, (CH<sub>3</sub>)<sub>2</sub>CHO<sub>2</sub>C), 4.49 (septet, *J* = 6.3 Hz, 1H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 2.88 (dd, *J* = 7.8, 7.4 Hz, 2H, CH<sub>2</sub>CO<sub>2</sub>*i*Pr), 2.57 (dd, *J* = 8.2, 7.4 Hz, 2H, ArCH<sub>2</sub>), 1.33 (d, *J* = 6.3 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 1.21 (d, *J* = 6.3 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>CHO<sub>2</sub>C). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 172.37, 153.50, 132.52, 131.81, 128.38, 127.67, 126.21 (d, *J*<sub>OC</sub> 5.4 Hz), 114.42, 113.76 (d, *J*<sub>OC</sub> = 8.3 Hz), 70.01 (d *J*<sub>OC</sub>, 3.4 Hz), 67.64 (d, *J*<sub>OC</sub> 11.2 Hz), 36.58, 30.40, 22.28, 21.93. HRMS Calcd for C<sub>17</sub>H<sub>24</sub>O<sub>3</sub>: 276.1725. Found: 276.1716. Anal. Calcd for C<sub>17</sub>H<sub>24</sub>O<sub>3</sub>: C, 73.88; H, 8.75. Found: C, 73.71; H, 8.73.

**Example 10: Synthesis of I -(*p*-isopropoxy-*m*-vinylphenyl)propionic acid (26).** A 100 mL round-bottom flask was charged with isopropyl- 1 -(*p*-isopropoxy-*m*-vinylphenyl)propionate (462 mg, 1.67 mmol) and 66.8 mL of 1 M KOH (66.8 mmol, 40 equiv). The reaction vessel was equipped with a condenser and heated at 100 °C for 12 h. The mixture was then diluted with 100 mL of water, transferred to a 500 mL Erlenmeyer flask, and cooled to 0 °C. The mixture was neutralized by the dropwise addition of ice-cold 1 M HCl. At a pH of ~7, 150 mL of Et<sub>2</sub>O was added. The aqueous layer was acidified further to pH 3-4 with vigorous stirring, resulting in spontaneous precipitation of the product that immediately enters the organic phase. The layers were partitioned in a separatory funnel (an emulsion may form, requiring extended time for phase separation), and the aqueous layer was washed with additional Et<sub>2</sub>O (150 mL). The pH of the aqueous layer was then lowered to ~2 in the presence of Et<sub>2</sub>O. Again, the organic layer was collected and the aqueous layer was washed. The organic layers were

pooled and washed with 500 mL of a saturated solution of sodium chloride. Drying over  $\text{MgSO}_4$  and concentration in vacuo afforded 355 mg (1.52 mmol, 91%) of a light yellow solid which proved to be >98% pure as judged by  $^1\text{H}$  NMR spectroscopy (400 MHz). If necessary, the acid could be further purified by silica gel chromatography (TLC  $R_f$  = 0.31 in 3:2 hexanes: $\text{Et}_2\text{O}$ ). It is recommended that the above procedure be followed with care since the product is quite prone to acid-catalyzed polymerization of the styrene moiety. Rapid, uncontrolled addition of the acid or acidification in the absence of  $\text{Et}_2\text{O}$  can result in complete loss of the product to polymerization. IR (NaCl): 2979 (m), 2935 (w), 2860 (w), 2760 (w), 1686 (s), 1600 (s), 1243 (s).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  11.26 (br, 1H,  $\text{CO}_2\text{H}$ ), 7.32 (d,  $J$  = 2.3 Hz, 1H, aromatic CH), 7.06-7.00 (m, 2H, aromatic CH and  $\text{ArCHCH}_2$ ), 6.81 (d,  $J$  = 8.5 Hz, 1H, aromatic CH), 5.72 (dd,  $J$  = 17.8, 1.5 Hz, 1H,  $\text{ArCHCH}_2$ ), 5.23 (dd,  $J$  = 11.0, 1.5 Hz, 1H,  $\text{ArCHCH}_2$ ), 4.50 (septet,  $J$  = 6.1 Hz, 1H,  $(\text{CH}_3)_2\text{CHOAr}$ ), 2.90 (dd,  $J$  = 8.0, 7.6 Hz, 2H,  $\text{CH}_2\text{CO}_2i\text{Pr}$ ), 2.67 (dd,  $J$  = 8.0, 7.6 Hz, 2H,  $\text{ArCH}_2$ ), 1.34 (d,  $J$  = 6.2 Hz, 6H,  $(\text{CH}_3)_2\text{CHOAr}$ ).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  178.78, 153.77, 132.13, 131.88, 128.40, 127.87, 126.29, 114.48, 113.99, 70.99, 35.80, 29.88, 22.19. HRMS Calcd for  $\text{C}_{14}\text{H}_{18}\text{O}_3$ : 234.1256. Found: 234.1257. Anal. Calcd for  $\text{C}_{14}\text{H}_{18}\text{O}_3$ : C, 71.77; H, 7.74. Found: C, 71.71; H, 7.68.

**Example 11: Synthesis of Tetraallylsilane (27).** A 250 mL 2-neck flask equipped with a condenser and addition funnel was charged with freshly prepared allylmagnesium bromide in  $\text{Et}_2\text{O}$  (92.3 mL of a 0.95 M solution, 87.7 mmol, 4.1 equiv).  $\text{SiCl}_4$  (2.45 mL, 21.4 mmol) was slowly added to the solution of Grignard reagent through the addition funnel in 20 mL of  $\text{Et}_2\text{O}$  at 22 °C over the course of 1 h. After 12 h of reflux at 35 °C, the reaction was cooled to 0 °C and quenched with 10 mL of a saturated solution of ammonium chloride. The mixture was diluted with water (200 mL) and  $\text{Et}_2\text{O}$  (100 mL) and transferred to a separatory funnel. The organic layer was collected and the aqueous layer was washed with 2 x 150 mL of  $\text{Et}_2\text{O}$ . The organic layers were dried over  $\text{MgSO}_4$ , filtered, and concentrated in vacuo into a colorless oil. This material was passed through a small plug of silica in hexanes (TLC  $R_f$  = 0.9 in hexanes) and

concentrated. Vacuum distillation afforded 3.33 g (17.3 mmol, 81%) of the product as a colorless oil. IR (NaCl): 3078 (m), 3060 (w), 2996 (w), 2972 (m), 2916 (w), 2882 (w), 1630 (s), 1419 (m), 1393 (m), 1195 (m), 1154 (m), 1037 (m), 991 (s), 930 (m), 893 (s), 810 (m), 601 (m).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.80 (ddt,  $J = 16.8, 10.2, 8.2$  Hz, 4H,  $\text{CH}=\text{CH}_2$ ), 4.94-4.87 (m, 8H,  $\text{CH}=\text{CH}_2$ ), 1.61 (ddd,  $J = 8.2, 1.4, 1.0$  Hz, 8H,  $\text{SiCH}_2$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  134.07, 113.93, 19.03. Anal. Calcd for  $\text{C}_{12}\text{H}_{20}\text{Si}$ : C, 74.92; H, 10.48. Found: C, 75.01; H, 10.32.

**Example 12: Synthesis of  $\text{Si}[(\text{CH}_2)_3\text{Si}(\text{Me})_2\text{CH}=\text{CH}_2]_4$  (28).** A 0.1 M solution of  $\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$  (Speier's catalyst)<sup>34</sup> was freshly prepared in anhydrous 2-propanol. The hydrosilylation could also be effected with Karstedt's catalyst.<sup>35</sup> A 25 mL round-bottom flask was charged with the tetraene (27) (762 mg, 3.96 mmol),  $\text{HMe}_2\text{SiCl}$  (2.00 mL, 18.0 mmol, 4.6 equiv), and THF (0.5 M, 8.0 mL). The platinum catalyst (10.0 mL, 0.010 mmol, 0.0025 equiv) was added dropwise by syringe and the colorless solution was heated at reflux (65 °C) for 12 h. After 20 mm of reaction, the mixture had turned dark green in color. Reaction progress was monitored readily by thin-layer chromatography; the starting material (TLC  $R_f = 0.9$  in hexanes) stains bright yellow with  $\text{KMnO}_4$ . Following the removal of solvent and excess silane in vacuo,  $^1\text{H}$  NMR analysis (400 MHz) of the unpurified mixture indicated that <5% of the  $\alpha$ -substituted product was present and that the material was sufficiently pure for the subsequent alkylation step. Thus, the product was dissolved in 20 mL of  $\text{Et}_2\text{O}$  and transferred by cannula into a solution of freshly prepared allylmagnesium bromide (0.936 M, 17.8 mL, 16.7 mmol, 4.2 equiv). The reaction was stirred for 12 h at 22 °C and quenched with 10 mL of a saturated solution of ammonium chloride. The mixture was diluted with water (200 mL) and  $\text{Et}_2\text{O}$  (150 mL) and partitioned in a separatory funnel. The aqueous layer was washed with 2 x 100 mL of  $\text{Et}_2\text{O}$ . The combined organic layers were washed with a volume of saturated sodium chloride, dried over  $\text{MgSO}_4$ , and vacuum filtered through a coarse frit funnel containing celite. Removal of volatiles gave a crude light orange oil which was purified by silica gel chromatography (TLC  $R_f = 0.63$  in

hexanes). The product was recovered as a colorless oil (2.11 g, 3.56 mmol, 90%). IR (NaCl): 3077 (w), 2954 (m), 2913 (s), 2876 (m), 1630 (m), 1418 (w), 1250 (s), 1153 (m), 1034 (w), 990 (w), 932 (w), 893 (s), 844 (s), 698 (w), 629 (w).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.78 (ddt,  $J$  = 16.8, 10.2, 8.2 Hz, 4H,  $\text{CH}=\text{CH}_2$ ), 4.87–4.79 (m, 8H,  $\text{CH}=\text{CH}_2$ ), 1.51 (d,  $J$  = 8.2 Hz, 8H,  $\text{SiCH}_2\text{CH}=\text{CH}_2$ ), 1.32 (m, 8H,  $\text{SiCH}_2\text{CH}_2\text{CH}_2\text{Si}$ ), 0.62–0.53 (m, 16H,  $\text{SiCH}_2\text{CH}_2\text{CH}_2\text{Si}$ ), -0.02 (s, 24H,  $\text{Si}(\text{CH}_3)_2$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  135.21, 112.47, 23.49, 19.93, 18.55, 17.54, -3.52. HRMS Calcd for  $\text{C}_{32}\text{H}_{67}\text{Si}_5$ : 591.4089 (M-H)+. Found: 591.4072. Anal. Calcd for  $\text{C}_{32}\text{H}_{68}\text{Si}_5$ : C, 64.78; H, 11.55. Found: C, 64.98; H, 11.55.

**Example 13: Synthesis of  $\text{Ar}(\text{CH}_2)_2\text{CO}_2(\text{CH}_2)_3\text{Si}(\text{Me})_2(\text{CH}_2)_3\text{SiL}_4$  (29).**

10  $\text{Si}[(\text{CH}_2)_3\text{Si}(\text{Me})_2\text{CH}=\text{CH}_2]_4$  (28) (587 mg, 0.989 mmol) was weighed into a 50 mL round-bottom flask and dissolved in 10 mL of THF. This solution was treated by cannula with freshly prepared 9-BBN (527 mg, 4.69 mmol, 4.74 equiv) in 10 mL of THF. After 12 h of stirring at 22 °C, 10 mL each of  $\text{H}_2\text{O}_2$  (30% wt. solution in water), 2 M NaOH, and ethanol were added. The mixture was then allowed to stir an additional 12 h at 22 °C. Water (100 mL) and  $\text{Et}_2\text{O}$  (100 mL) were added and the organic layer was removed. The aqueous layer was washed with 2 x 100 mL of  $\text{Et}_2\text{O}$ . The combined organic layers were dried over  $\text{MgSO}_4$  and filtered. Removal of volatiles gave a crude oil that was purified by silica gel chromatography (TLC  $R_f$  = 0.36 in  $\text{EtOAc}$ ).  $^1\text{H}$  NMR analysis (400 MHz) indicated that the product contained minor impurities (including cyclooctadiol) which made characterization of the material difficult. Thus, the crude product was carried directly into the next step. The tetraol was transferred to a 25 mL round-bottom flask, dissolved in 15 mL of  $\text{CH}_2\text{Cl}_2$ , and cooled to 0 °C. 1-(*p*-isopropoxy-*m*-vinylphenyl)propionic acid (26) (1.02 g, 4.35 mmol, 4.4 equiv), EDC (912 mg, 4.76 mmol, 4.8 equiv), and DMAP (61 mg, 0.50 mmol, 0.50 equiv) were then directly added in succession to the mixture as solids. The resulting mixture was stirred for 4 h and quenched with 2 mL of a 10% citric acid solution. Additional water was added (200 mL) and the aqueous layer was washed with 3 x 100 mL of  $\text{Et}_2\text{O}$ . The combined organic layers were washed with 1 volume each of a

saturated solution of sodium chloride and water. Drying over  $\text{MgSO}_4$ , filtration, and concentration gave a crude oil which was purified by silica gel chromatography (TLC  $R_f$  0.36 in 4:1 hexanes:EtOAc). The desired tetra(ester) was recovered as a colorless oil (954 mg, 0.623 mmol, 63%). IR (NaCl): 2974 (m), 2951 (m), 2919 (s), 2873 (m), 2855 (m), 1735 (s), 1627 (w), 1491 (m), 1451 (w), 1384 (w), 1372 (w), 1293 (w), 1247 (s), 1139 (m), 1119 (m), 958 (w), 906 (w), 837 (m).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 87.30 (d,  $J$  = 2.4 Hz, 4H, aromatic CH), 7.02 (d,  $J$  = 6.4 Hz, 4H, aromatic CH), 7.02 (dd,  $J$  = 19.8, 9.4 Hz, 4H,  $\text{ArCHCH}_2$ ), 6.79 (d,  $J$  = 8.8 Hz, 4H, aromatic CH), 5.71 (dd,  $J$  = 17.8, 1.6 Hz, 4H,  $\text{ArCHCH}_2$ ), 5.21 (dd,  $J$  = 11.4, 1.6 Hz, 4H,  $\text{ArCHCH}_2$ ), 4.48 (septet,  $J$  = 6.2 Hz, 4H,  $(\text{CH}_3)_2\text{CHOAr}$ ), 4.01 (t,  $J$  = 7.0 Hz, 8H,  $\text{CO}_2\text{CH}_2$ ), 2.88 (t,  $J$  = 7.8 Hz, 8H,  $\text{ArCH}_2\text{CH}_2\text{CO}_2$ ), 2.59 (t,  $J$  = 7.8 Hz, 8H,  $\text{ArCH}_2\text{CH}_2\text{CO}_2$ ), 1.58 (m, 8H,  $\text{CO}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Si}(\text{Me})_2$ ), 1.36-1.25 (m, 8H,  $\text{SiCH}_2\text{CH}_2\text{CH}_2\text{Si}(\text{Me})_2$ ), 1.33 (d,  $J$  = 5.6 Hz, 24H,  $(\text{CH}_3)_2\text{CHOAr}$ ), 0.58-0.52 (m, 16H,  $\text{CH}_2\text{Si}(\text{Me})_2\text{CH}_2$ ), 0.47-0.42 (m, 8H,  $\text{Si}(\text{CH}_2)_4$ ), -0.04 (s, 24H,  $\text{Si}(\text{Me})_2$ ).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  172.77, 153.44, 132.40, 131.76, 128.30, 127.61, 126.14, 114.30, 113.78, 70.96, 67.16, 36.30, 30.38, 23.33, 22.33, 20.20, 18.65, 17.63, 11.30, -3.26. LRMS Calcd for  $\text{C}_{88}\text{H}_{140}\text{O}_{12}\text{Si}_5\text{K}$  (M+K): 1569.9. Found: 1569.5. Anal. Calcd for  $\text{C}_{88}\text{H}_{140}\text{O}_{12}\text{Si}_5$ : C, 69.06; H, 9.22. Found: C, 69.31; H, 9.36.

#### Example 14: Synthesis of $[(\text{PCy}_3)_2\text{Cl}_2\text{Ru}=\text{CH}-\text{o}-\text{O}-\text{i}-$

$\text{PrC}_6\text{H}_3(\text{CH}_2)_2\text{C}(\text{OOC}(\text{CH}_2)_3\text{Si}(\text{Me})_2\text{CH}_2\text{Si})_4$  (Formula 30).  $(\text{PCy}_3)_2\text{Cl}_2\text{Ru}=\text{CHPh}$  (2) (792 mg, 0.962 mmol, 4.3 equiv) and  $\text{CuCl}$  (106 mg, 1.07 mmol, 4.8 equiv) were added to a 25 mL round-bottom flask and suspended in 12 mL of  $\text{CH}_2\text{Cl}_2$ . Dendrimer **29** (341 mg, 0.223 mmol, 1.0 equiv) was added to this mixture through a cannula in 10 mL of  $\text{CH}_2\text{Cl}_2$ . The mixture was stirred for a period of 3 h at 22 °C, during which time the original purple solution turned dark brown in color. The following work-up procedures were conducted in air with reagent-grade solvents. The mixture was concentrated at reduced pressure and passed through a short plug of silica gel in 3:2 hexanes:Et<sub>2</sub>O (brown band rapidly elutes). Product fractions were pooled and concentrated. This material was passed through a second column of silica gel, this time with a



gradient elution (1:1 hexanes:CH<sub>2</sub>Cl<sub>2</sub> to 2:3 hexanes:CH<sub>2</sub>Cl<sub>2</sub> to 1:3 hexanes:CH<sub>2</sub>Cl<sub>2</sub> to 100% CH<sub>2</sub>Cl<sub>2</sub>). Finally, the column was flushed with Et<sub>2</sub>O, at which point the product elutes (brown band). Solvent removal afforded a dark brown crystalline solid (637 mg, 0.194 mmol, 87%). IR (NaCl): 2927 (s), 2852 (s), 1955 (w), 1733 (s), 1684 (w), 1610 (w), 1582 (w), 1488 (m), 1447 (m), 1417 (w), 1385 (m), 1296 (w), 1247 (m), 1222 (m), 1204 (m), 1134 (m), 1104 (m), 913 (w), 891 (w), 849 (m), 774 (w), 735 (m), 702 (w). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 6 17.38 (d, *J* = 4.0 Hz, 4H, Ru=CHAr), 7.52 (s, 4H, aromatic CH), 7.46 (d, *J* = 8.8 Hz, 4H, aromatic CH), 6.98 (d, *J* = 8.8 Hz, 4H, aromatic CH), 5.23 (septet, *J* = 6.2 Hz, 4H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 4.03 (t, *J* = 7.1 Hz, 8H, CO<sub>2</sub>CH<sub>2</sub>), 3.03 (t, *J* = 7.7 Hz, 8H, ArCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>), 2.64 (t, *J* = 7.7 Hz, 8H, ArCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>), 2.32 (m, 12H, PCH), 2.20-1.20 (m, 136H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si(Me)<sub>2</sub>, SiCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si(Me)<sub>2</sub>, and P(CH(CH<sub>2</sub>)<sub>5</sub>)<sub>3</sub>), 1 79 (d, *J* = 6.2 Hz, 24H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 0.60-0.52 (m, 16H, CH<sub>2</sub>Si(Me)<sub>2</sub>CH<sub>2</sub>), 0.50-0.45 (m, 8H, Si(CH<sub>2</sub>)<sub>4</sub>), -0.03 (s, 24H, Si(Me)<sub>2</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 8 279.24, 172.60, 151.29, 143.79, 134.69, 129.42, 122.51 (d, *J*<sub>OC</sub> = 5.9 Hz), 113.19, 75.50 (d, *J*<sub>OC</sub> = 7.8 Hz), 67.27, 36.36, 35.67 (d, *J*<sub>PH</sub> = 24.4 Hz), 30.14, 29.73, 27.80 (d, *J*<sub>PH</sub> = 10.7 Hz), 26.33, 23.26, 22.14, 20.14, 18.58, 17.56, 11.26, -3.33. <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>): 859.17 (s, PCy<sub>3</sub>). LRMS Calcd for C<sub>156</sub>H<sub>264</sub>Cl<sub>8</sub>O<sub>12</sub>P<sub>4</sub>Ru<sub>4</sub>Si<sub>5</sub>Na<sub>2</sub> (M+2Na)<sup>+</sup>: 3331.2. Found: 3331.8. Anal. Calcd for C<sub>156</sub>H<sub>264</sub>Cl<sub>8</sub>O<sub>12</sub>P<sub>4</sub>Ru<sub>4</sub>Si<sub>5</sub>: C, 57.05; H, 8.10. Found: C, 56.80; H, 8.00.

**Example 15: Synthesis of [(4,5 - dihydrolMES) Cl<sub>2</sub> Ru = CH-o-O-i-**

**PrC<sub>6</sub>H<sub>3</sub>(CH<sub>2</sub>)<sub>2</sub>C00(CH<sub>2</sub>)<sub>3</sub>Si(Me)<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>Si]<sub>4</sub>** (formula 31). The unmetallated dendrimer (29) (227mg, 0.148 mmol, 1.0 equiv) was weighed into a 25 mL round-bottom flask and dissolved in 15 mL of CH<sub>2</sub>Cl<sub>2</sub>. (4,5-dihydrolMES)(PCy<sub>3</sub>)Cl<sub>2</sub>Ru=CHPh (3) (606 mg, 0.714 mmol, 4.8 equiv) and CuCl (72.0 mg, 0.731 mmol, 4.9 equiv) were added directly to this solution as solids. The mixture was stirred for 2 h at 22 °C, during which time the original purple solution turned a dark green/brown color. The following work-up procedures were conducted in air using reagent grade solvents. The mixture was concentrated at reduced pressure and passed through a short column of silica gel using a gradient elution (100% CH<sub>2</sub>Cl<sub>2</sub> to 4:1 hexanes:Et<sub>2</sub>O to 1:1 hexanes:

Et<sub>2</sub>O to 100% Et<sub>2</sub>O). The green band was collected and concentrated, affording a green microcrystalline solid (277 mg, 0.0816 mmol, 55%). IR (NaCl): 3432 (b), 2915 (m), 1732 (s), 1632 (w), 1607 (w), 1595 (w), 1487 (s), 1418 (m), 1259 (s), 1221 (m), 1132 (m), 1104 (m), 1034 (w), 912 (w), 849 (w), 579 (w). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 16.51 (s, 4H, Ru=CHAr), 7.33 (d, *J* = 7.0 Hz, 4H, aromatic CH), 7.07 (s, 16H, mesityl aromatic CH), 6.74-6.66 (m, 8H, aromatic CH), 4.85 (septet, *J* = 6.3 Hz, 4H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 4.17 (s, 16H, N(CH<sub>2</sub>)<sub>2</sub>N), 4.02 (t, *J* = 7.0 Hz, 8H, CO<sub>2</sub>CH<sub>2</sub>), 2.91 (t, *J* = 7.8 Hz, 8H, ArCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>), 2.53 (t, *J* = 7.8 Hz, 8H, ArCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>), 2.47 (s, 48H, mesityl *o*-CH<sub>3</sub>), 2.41 (s, 24H, mesityl *p*-CH<sub>3</sub>), 1.61 (m, 8H, CO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si(Me)<sub>2</sub>), 1.40-1.25 (m, 8H, SiCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Si(Me)<sub>2</sub>), 1.24 (d, *J* = 6.3 Hz, 24H, (CH<sub>3</sub>)<sub>2</sub>CHOAr), 0.61-0.45 (m, 24H, CH<sub>2</sub>Si(Me)<sub>2</sub>CH<sub>2</sub> and Si(CH<sub>2</sub>)<sub>4</sub>), -0.02 (s, 24H, Si(Me)<sub>2</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 297.07 (d, *J* = 166.0 Hz), 211.32, 172.81, 150.80, 145.16, 138.76, 134.28, 130.42, 130.29, 129.80, 129.39, 128.74, 128.22, 74.41, 67.19, 51.44, 36.03, 29.54, 23.14, 21.53, 20.96, 20.60, 20.03, 18.48, 17.47, 11.12, -4.13. LRMS Calcd for C<sub>168</sub>H<sub>240</sub>Cl<sub>8</sub>N<sub>8</sub>O<sub>12</sub>Ru<sub>4</sub>Si<sub>5</sub> (M+4H): 3393.1. Found: 3393.1. Anal. Calcd for C<sub>168</sub>H<sub>236</sub>Cl<sub>8</sub>N<sub>8</sub>O<sub>12</sub>Ru<sub>4</sub>Si<sub>5</sub>: C, 59.56; H, 7.02. Found: C, 59.55; H, 6.96.

#### Example 16: Representative Experimental Procedure for RCM Catalyzed by

**Monomer (4,5 dihydrolMES)Cl<sub>2</sub>Ru=CH-*o*-*o*-*i*-PrC<sub>6</sub>H<sub>4</sub> (formula 5).** Triene (7) (50.1 mg, 0.329 mmol, 1.0 equiv) was weighed out in a 25 mL round-bottom flask and dissolved in 3 mL of CH<sub>2</sub>Cl<sub>2</sub> (0.1 M). (4,5-dihydrolMES)Cl<sub>2</sub>RuCH-*o*-*o*-*i*-PrC<sub>6</sub>H<sub>4</sub> (5) (9.80 mg, 0.0156 mmol, 0.0474 equiv) was added as a solid and the resulting deep green solution was stirred at 22 °C. TLC analysis after 10 mm indicated completion of the reaction. As usual, work-up procedures were conducted in air using reagent-grade solvents. The mixture was concentrated at reduced pressure and passed through a short column of silica gel in 2:1 hexanes:CH<sub>2</sub>Cl<sub>2</sub> affording diene (8) (33.4 mg, 0.269 mmol, 82%) as a colorless oil (TLC R<sub>f</sub> = 0.46 in 9:1 hexanes:Et<sub>2</sub>O). The catalyst was then retrieved as a green solid by flushing the silica column with 100% CH<sub>2</sub>Cl<sub>2</sub> (9.60 mg, 0.0153 mmol, 98%).

**Example 17: Representative Experimental Procedure for RCM Catalyzed by Dendritic [(PCY<sub>3</sub>)Cl<sub>2</sub>Ru=CH-*o*-0-*i*-PrC<sub>6</sub>H<sub>3</sub>(CH<sub>2</sub>)<sub>2</sub>COO(CH<sub>2</sub>)<sub>3</sub>Si(Me)<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>Si]<sub>4</sub> (formula 30).**

Tosyl amide (32) (250 mg, 0.995 mmol, 1.0 equiv) and dendritic catalyst (30) (43.9 mg, 0.0140 mmol, 0.014 equiv) were weighed into a 50 mL round-bottom flask. The flask was equipped

5 with a reflux condenser, evacuated, and filled with an atmosphere of argon. The vessel was charged with CH<sub>2</sub>Cl<sub>2</sub> (20 mL, 0.05 M) and submerged into an oil bath preheated to 45 °C. The reaction was stirred for 15 minutes, at which point TLC analysis indicated completion of the reaction. Removal of the solvent in vacuo afforded a dark brown oil that was purified by silica gel chromatography (100% CH<sub>2</sub>Cl<sub>2</sub>), affording 33 as a white solid (219 mg, 0.983 mmol, 99%).

10 The column was then flushed with 100% Et<sub>2</sub>O to recover the dendritic catalyst as a brown solid residue (46.2 mg, 0.0141 mmol, 100%). The recovered catalyst was transferred directly into a new flask for a subsequent reaction. As discussed above, Ru recovery on the dendrimer could be quickly analyzed upon inspection of the <sup>1</sup>H NMR (400 MHz) spectrum. Integration of the benzylic methylene protons at 3.03 ppm (metal-occupied sites) and 2.88 ppm (metal-vacant sites)

15 provided a ratio of 88:12 respectively.

**Example 18: Experimental Procedure for RCM Catalyzed by Dendritic [(4,5-dihydrolMES)C<sub>12</sub>Ru=CH-*o*-0-*i*-PrC<sub>6</sub>H<sub>3</sub>(CH<sub>2</sub>)<sub>2</sub>COO(CH<sub>2</sub>)<sub>3</sub>Si(Me)<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>Si]<sub>4</sub> (formula 31).**

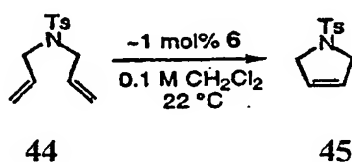
Diene (11) (32.7 mg, 0.233 mmol, 1.0 equiv) was weighed into a 25 mL round-bottom flask and dissolved in 5 mL of CH<sub>2</sub>Cl<sub>2</sub> (0.05 M). Dendritic catalyst 31 (12.4 mg, 0.00366 mmol, 0.016 equiv) was added as a solid and the solution was allowed to stir at 22 °C. TLC analysis after 2 h

20 indicated completion of the reaction. Work-up procedures proceeded in air with reagent-grade solvents. The mixture was concentrated at reduced pressure and passed through a short plug of silica gel in 100% CH<sub>2</sub>Cl<sub>2</sub>, affording (12) (20.4 mg, 0.1819 mmol, 78%) as a colorless oil (TLC R<sub>f</sub> = 0.25 in 4:1 hexanes:Et<sub>2</sub>O). The catalyst was then flushed off of the column with 100% Et<sub>2</sub>O

25 affording 12.3 mg (0.00363 mmol, 99%) of a green solid. Ru recovery on the dendrimer was assessed using <sup>1</sup>H NMR spectroscopy (400 MHz). Integration of the isopropoxy methine proton

for both metal-occupied (4.90 ppm) and metal-vacant (5.71 ppm) sites gave a ratio of 92:8 respectively, indicative of 8% metal loss.

**Example 19: Synthesis of an Immobilized Catalyst.** This procedure allows installment of the linker and the active metal complex in a single step. Treatment of the compound **3** with a stoichiometric amount of (4,5-dihydroIMES)(PC<sub>3</sub>)<sub>3</sub> Cl<sub>2</sub>Ru=CHPh in the presence of allylchlorodimethylsilane led to successful ring-opening cross metathesis and metallation of the styrenyl ether “docking site.” Subsequent diffusion of this product into the pores of a sol gel sample (200 Å pore size glass monoliths, available from Geltech, Orlando, FLA.) resulted in a substitution reaction involving the labile Si-Cl bond with the free hydroxyl groups on the glass surface. After extensive washing and drying *in vacuo*, a bright green glass pellet (Formula 6) was recovered which showed good activity in the RCM of the terminal diene **44** (0.10 mmol scale) to yield **45** (as shown in Scheme 7). The immobilized catalyst was then carried through three iterative rounds of metathesis to convert diene **44** to the cyclic compound **45** as shown below.



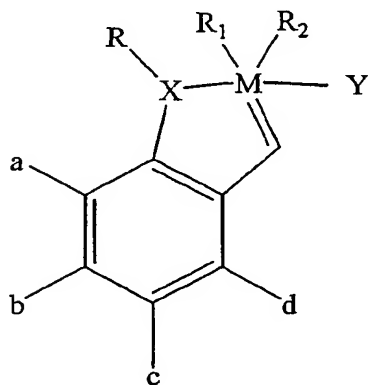
Although successive ring-closures required longer reaction times, >90% conversion was observed in each case, the following factors were observed: (1) Derivatization of the sol gel pellet resulted in a 1.0 mg increase in mass. Calculations therefore suggest that the RCM of compound 7 was mediated by a very small amount of active catalyst (~ 1 mol%). This may partly account for the slow reaction rate, particularly in the second and third cycles. Increasing the catalyst loading to 5 mol% will lead to dramatic improvements in reaction rate. (2) In contrast to reactions run with 5 mol% Formula 1 or 5, the spectrum of the unpurified reaction

mixture consisted of > 98% pure cycloolefin (no catalyst or byproduct thereof could be detected). (3) No filtration step was required to isolate the product. The reaction mixture was simply removed with a Pasteur pipette, the glass sample was washed with  $\text{CH}_2\text{Cl}_2$ , and fresh substrate was added.

- 5           Although the invention has been described in detail for the purpose of illustration, it is understood that such detail is solely for this purpose, and variations can be made therein by those skilled in the art without departing from the spirit and scope of the invention as described by the appended claims.

What is claimed is:

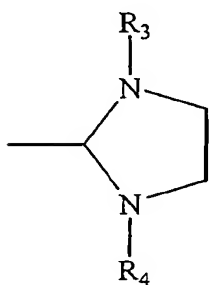
1. A composition comprising a transition metal catalyst having the following structure:



wherein:

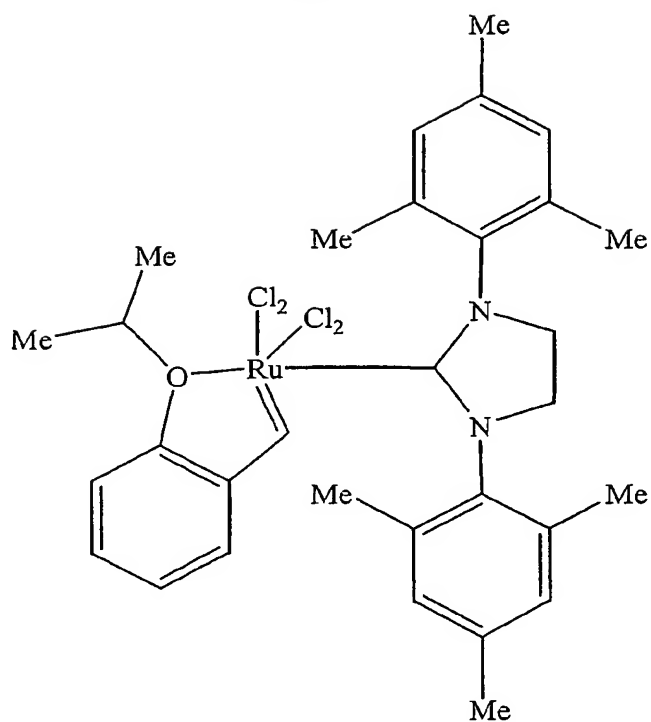
- 5 M comprises a transition metal; R comprises an alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, alkoxy carbonyl, alkylamino, alkylthio, alkylsulfonyl, alkylsulfinyl; each optionally substituted with an alkyl, halogen, alkoxy, aryl or heteroaryl moiety; R<sub>1</sub> and R<sub>2</sub> each comprises, or together comprise, an electron withdrawing anionic ligand; a, b, c, and d each comprises H, a halogen atom or an alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, alkoxycarbonyl, alkylamino, alkylthio, alkylsulfonyl; alkylsulfinyl; each optionally substituted with an alkyl, halogen, aryl or heteroaryl moiety; and Y comprises an electron-donating heterocyclic carbene ligand.
2. The composition of claim 1 wherein M is Ru.
3. The composition of claim 1 wherein X is O.
- 15 4. The composition of claim 1 wherein R is a lower alkyl group.
5. The composition of claim 4 wherein R is isopropyl.
6. The composition of claim 1 wherein R<sub>1</sub> and R<sub>2</sub> each is a halogen.

7. The composition of claim 6 wherein  $R_1$  and  $R_2$  each is Cl.
8. The composition of claim 1 wherein a, b, c, and d each comprises H or a lower alkyl group.
9. The composition of claim 1 wherein Y comprises a 4,5-dihydroimidazol-2-ylidene.
- 5 10. The composition of claim 9 wherein Y comprises a tricyclic aromatic ring structure having the following structure:



wherein  $R_3$  and  $R_4$  each comprises an aromatic ring moiety.

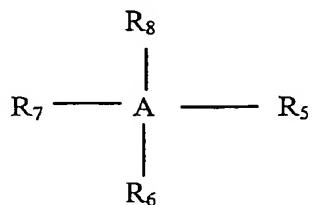
11. The composition of claim 10 wherein  $R_3$  and  $R_4$  comprise both comprise 2,4,6-trimethylphenyl (mesityl) moieties.
- 10
12. The composition of claim 1 comprising the following structure:



13. A composition of claim 1 wherein the transition metal catalyst is part of a dendrimer compound.

14. The transition metal catalyst of claim 13 having the following structure:

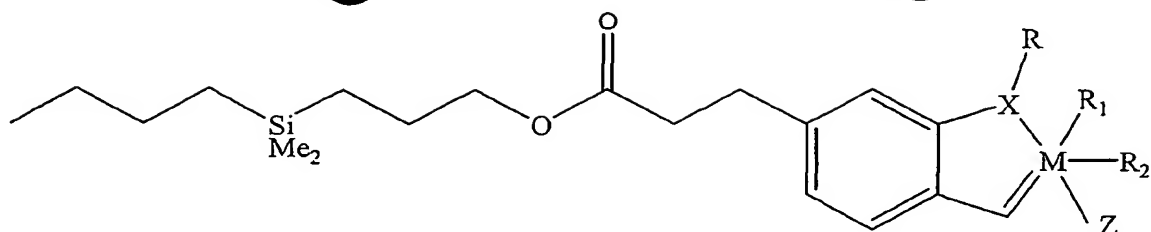
5



wherein A is a polyvalent atom selected from the group consisting of carbon, nitrogen, silicon  
 10 and phosphorous;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> each comprises the following structure:





wherein:

M comprises a transition metal;

X comprises O, S, N or P;

- 5        R comprises an alkyl, alkenyl, alkynyl, aryl, alkoxy, alkenyloxy, alkynyloxy, aryloxy, alkoxy carbonyl, alkylamino, alkylthio, alkylsulfonyl, alkylsulfinyl; each optionally submitted with an alkyl, halogen, aryl or heteroaryl moiety;

R<sub>1</sub> and R<sub>2</sub> each comprises, or together comprise, an electron withdrawing group; and

Z comprises Y or a phosphine group.

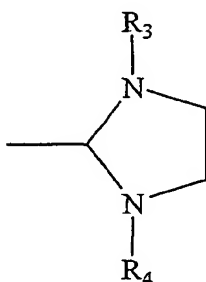
- 10    15.    The composition of claim 14 wherein A is silicon.
16.    The composition of claim 14 wherein M is a transition metal.
17.    The composition of claim 14 wherein M is ruthenium
18.    The composition of claim 14 wherein X is O.
19.    The composition of claim 14 wherein R is a lower alkyl group.
- 15    20.    The composition of claim 19 wherein R is isopropyl.
21.    The composition of claim 14 wherein R<sub>1</sub> and R<sub>2</sub> each is a halogen.
22.    The composition of claim 21 wherein R<sub>1</sub> and R<sub>2</sub> each is Cl.

23. The composition of claim 14 wherein Z comprises a phosphine moiety having the formula  $P(Cy)_3$ .

24. The composition of claim 23 wherein Cy comprises an aliphatic ring structure.

25. The composition of claim 23 wherein Cy comprises a cyclohexyl or cyclopentyl group.

26. The composition of claim 14 wherein Z comprises an aromatic ring structure having the following structure:

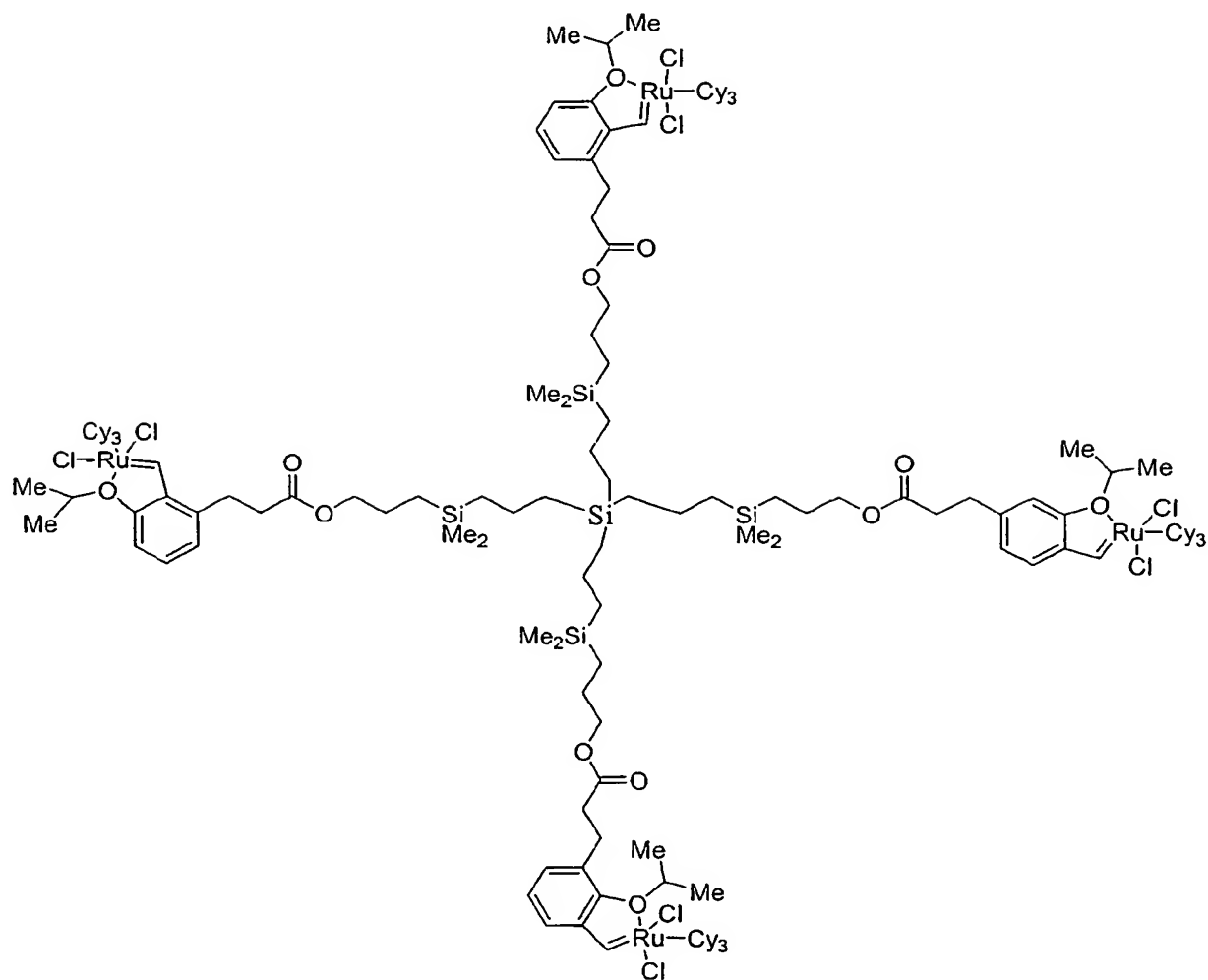


wherein: R<sub>3</sub> and R<sub>4</sub> each comprises an aromatic ring moiety.

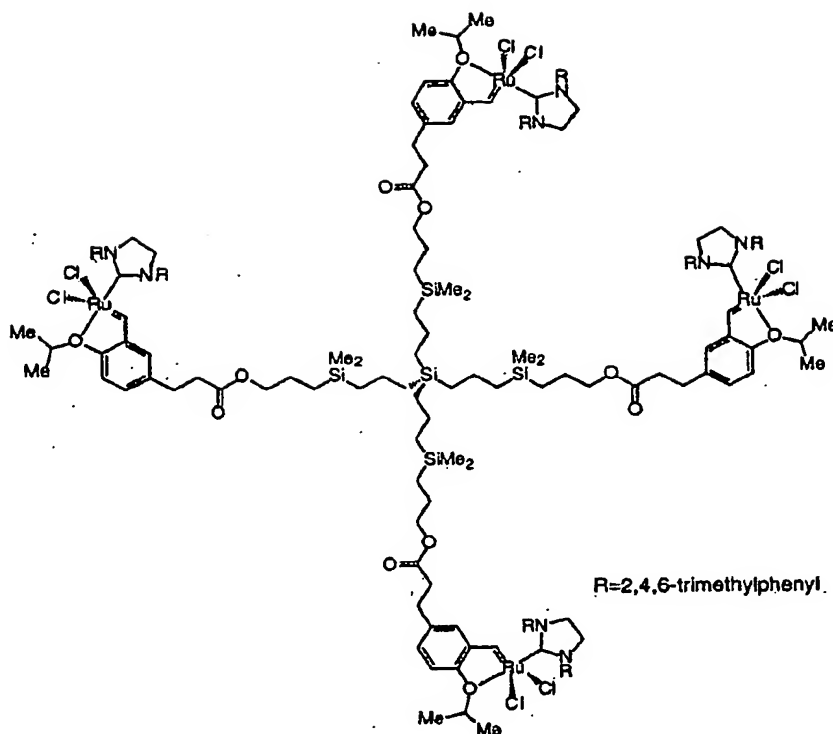
27. The composition of claim 26 wherein R<sub>3</sub> and R<sub>4</sub> each comprises 2, 4, 6-trimethylphenyl

(mesityl).

28. The composition of claim 14 comprising the following structures:



or



29. The composition of claim 1 wherein the transition metal catalyst is part of a polymeric compound.

30. The composition of claim 1 wherein the transition metal catalyst is chemically bound to a substrate surface.

31. The transition metal catalyst of claim 30 comprising at least one substituent that is capable of reacting with functional groups on the substrate surface so as to render the said catalyst chemically bonded to the said substrate surface.

32. The transition metal catalyst of claim 31 wherein the substituent is selected from the

group consisting of alkyl halosilanes, akenyl halosilanes, alkoxy halosilanes, aryloxy halosilanes, aryl halosilanes, alkyl halides, cycloalkyl halides, alkenyl halides, cycloalkenyl halides, aromatic and heteroaromatic halides, acid chlorides, anhydrides, succinidyl esters, epoxides, thiols, acrylate, methacrylate, acrylamide, methacrylamide, benzophenone, and derivatives thereof.

33. The transition metal catalyst of claim 32 wherein the substituent is alkylldimethylsilylchloride.
34. A composition of claim 1 wherein the said catalyst is capable of chemically bonding to a substrate surface.
- 5 35. A composition of claim 30 wherein the substrate is a porous or a non-porous solid phase.
36. A composition of claim 30 wherein the substrate is glass, metal, non-metal, ceramics, rubber or a polymeric material.
37. A composition of claim 30 wherein the substrate is part of a containing vessel.
38. A composition of claim 37 wherein the containing vessel is a chemical reactor..
- 10 39. A method of immobilizing the transition metal catalyst of claim 1 comprising the steps of
- i) reacting the said catalyst with a chemical coupling agent under conditions to form an adduct with said catalyst so as to render it capable of attachment to a substrate surface, and
- ii) contacting said adduct with a substrate or a substrate surface under conditions to
- 15 cause said adduct to become chemically bound to said substrate surface through covalent chemical bonding, ionic bonding, non-ionic interaction, or combinations thereof.
40. A method of claim 39 wherein the catalyst is a transition metal catalyst capable of reacting with a chemical coupling agent that is chemically bonded to a substrate surface.
- 20 41. A method of claim 40 wherein the chemical coupling agent comprises a compound containing at least one alkyl halosilanes, akenyl halosilanes, alkoxy halosilanes, aryloxy halosilanes and aryl halosilanes, akyl and cycloalkyl halides, alkenyl and cycloalkenyl halides,

aromatic and heteroaromatic halides, acid chlorides, anhydrides, succinimidyl esters, epoxides and thiols.

42. The method of claim 41 wherein the chemical coupling agent is allylchloro-dimethylsilane.

5 43. The method of claim 39 wherein the said transition metal catalyst is reacted with a plurality of chemically different coupling agents.

44. The method of claim 39 wherein the substrate is glass, metal, non-metal, ceramics, rubber or a polymeric material.

45. The method of claim 39 wherein the said substrate material is a porous or non-porous  
10 material.

46. The method of claim 45 wherein the said substrate material is a porous sol-gel.

47. The method of claim 45 wherein the said substrate material is a solid phase inorganic gel.

48. The method of Claim 47 wherein the said substrate material is a glass mono-lithic gel.

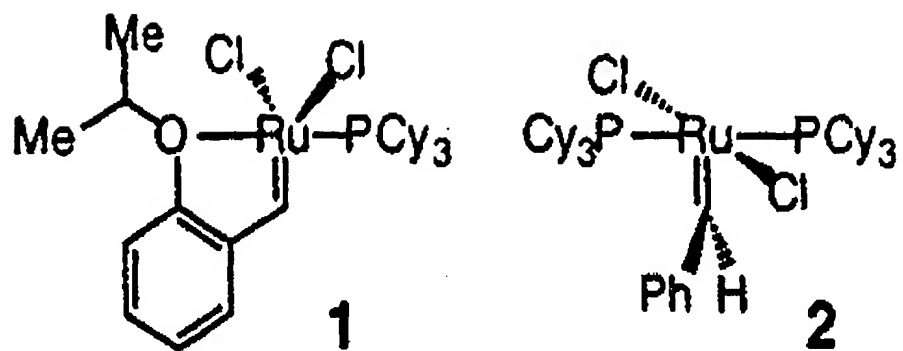
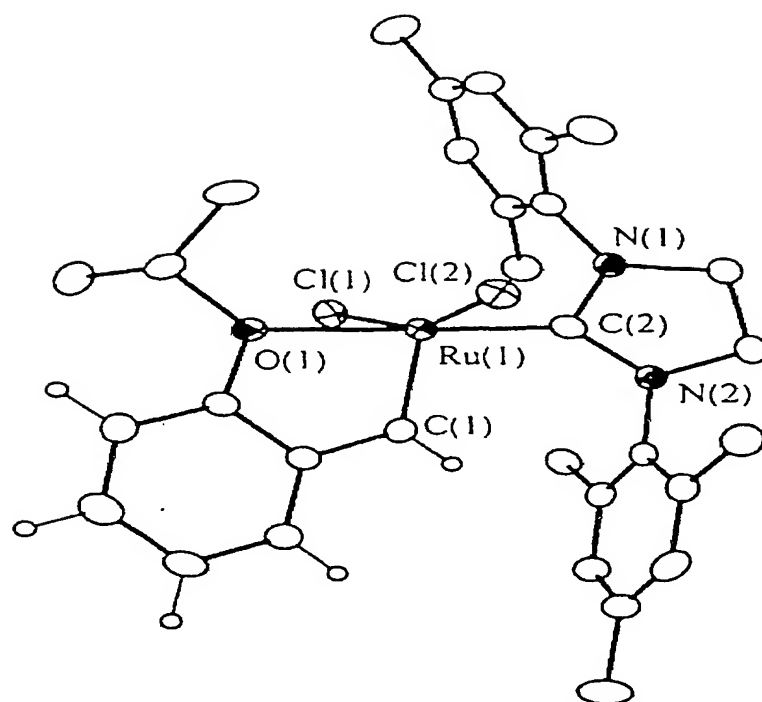


Figure 1

**Figure 2**



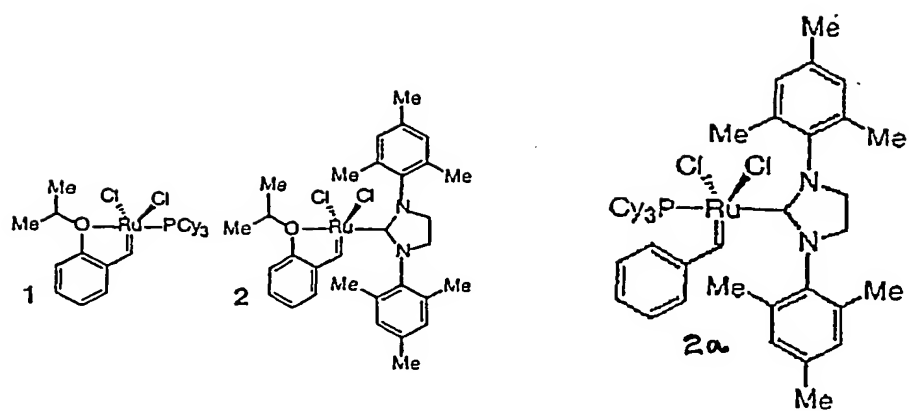


Figure 3

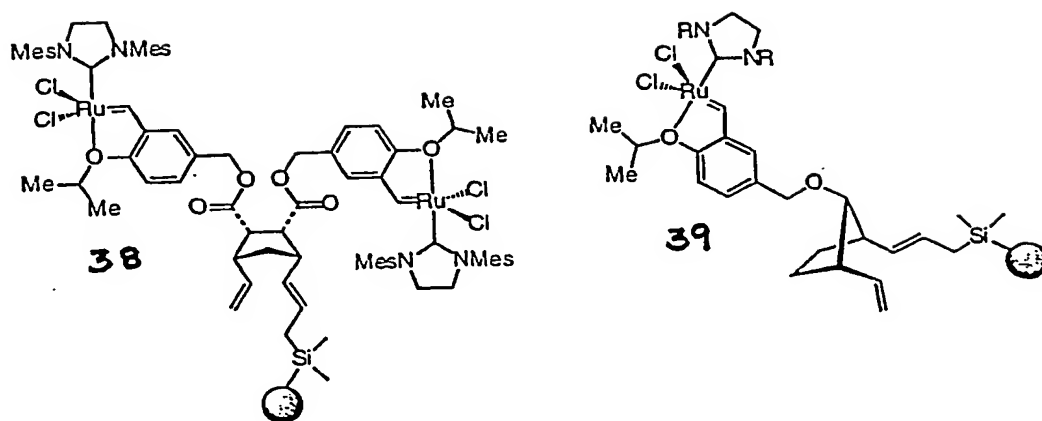


Figure 4

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(54) Title: RECYCLABLE METATHESIS CATALYSTS

(57) Abstract: Highly active, recoverable and recyclable transition metal-based metathesis catalysts and their organometallic complexes including dendrimeric complexes are disclosed, including a Ru complex bearing a 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene and styrenyl ether ligand. The heterocyclic ligand significantly enhances the catalytic activity, and the styrenyl ether allows for the easy recovery of the Ru complex. Derivatized catalysts capable of being immobilized on substrate surfaces are also disclosed. The present catalysts can be used to catalyze ring-closing metathesis (RCM), ring-opening (ROM) and cross metatheses (CM) reactions, and promote the efficient formation of various trisubstituted olefins at ambient temperature in high yield.

WO 02/014376 A3

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US01/24955

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : B01J 31/00; C07F 7/08, 9/28, 15/00 US CL : 502/158, 162, 167; 548/103; 556/12, 22, 23 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 502/158, 162, 167; 548/103; 556/12, 22, 23 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) REGISTRY and CAPLUS Databases		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HARRITY et al. Chromenes through Metal-Catalyzed Reactions of Styrenyl Ethers, Mechanism and Utility in Synthesis. Journal of American Chemical Society. 18 March 1998, vol. 120, no. 10, pages 2343-2351, see entire document.	1-13
A	KINGSBURY et al. A Recyclable Ru-based Metathesis Catalyst. Journal of American Chemical Society. 03 February 1999, vol. 121, no. 4, pages 791-799, see entire document.	1-13
X, P	GARBER et al. Efficient and recyclable Monomeric and Dendritic Ru-Based Metathesis Catalysts. Journal of American Chemical Society. 30 August 2000, vol. 122, no. 34, pages 8186-8179, see entire document.	1-48
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Date of the actual completion of the international search  29 OCTOBER 2001	Date of mailing of the international search report  <b>06 FEB 2002</b>	
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-8230	Authorized officer <i>James Ford</i> Porfirio Nazario-Gonzalez Telephone No. (703) 308-1235	

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/24955

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	GESSLER et al. Synthesis and metathesis reactions of a phosphine-free dihydroimidazole carbene ruthenium complex. Tetrahedron Letters, 16 december 2000, Vol. 41, No. 51, pages 9973-9976, particularly compound 6 on page 9974.	1-13
X, P	RANDL et al. Highly Selective Cross Metathesis with Acrylonitrile Using a Phosphine Free Ru-Complex. Synlett, 2001, No. 3, pages 430-432, particularly compound 3.	1-13

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